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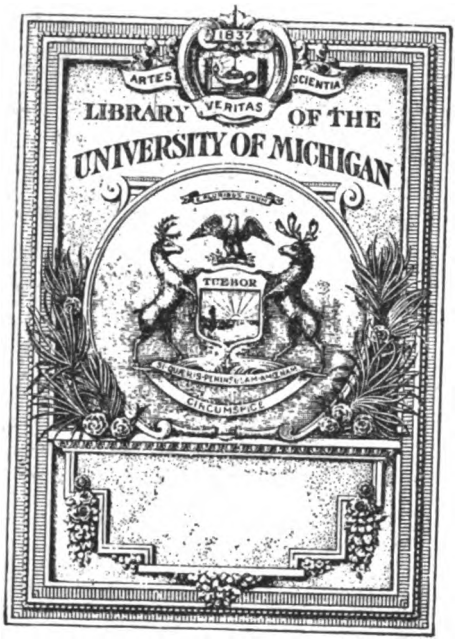

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THE PATHOLOGY OF THE PNEUMONIA IN THE UNITED STATES ARMY CAMPS DURING THE WINTER OF 1917–18.*

By WILLIAM G. MacCALLUM, M.D.,

Contract Surgeon, U. S. Army.

(*From the Pathological Department of Johns Hopkins University, Baltimore.*)

PLATES 1 TO 53.

(Received for publication, August 15, 1918.)

I. HISTORICAL SURVEY.

The gathering together of great numbers of men in the United States Army camps furnished conditions for an extensive outbreak of measles which was quickly followed by a rather unfamiliar form of pneumonia.

The Geographical and Historical Pathology of Hirsch, the volume on Epidemics in Haeser's History of Medicine, and other standard books that treat of the history of disease show that this is only one of a great number of epidemics of pneumonia which have been recorded

* These studies have grown out of the work of two Commissions sent out by the Surgeon General of the United States Army for the investigation of epidemics of pneumonia among the troops. The first Commission was composed of Rufus Cole, W. G. MacCallum, Oswald T. Avery, Contract Surgeons, United States Army, Captains A. R. Dochez and R. A. Kinsella, and Lieutenants F. G. Blake, T. M. Rivers, William C. von Glahn, J. John, and F. A. Stevens. The preliminary report of the activities at Fort Sam Houston, Texas, during February and March appeared in *The Journal of the American Medical Association*, 1918, lxx, 1146. The second Commission, which was composed of W. G. MacCallum, Contract Surgeon, Captain A. W. Sellards, and Lieutenants H. M. Thomas, Jr., and A. B. Lyons, worked at Camp Dodge, Iowa, during May, 1918. A brief summary of the activities of this Commission was presented at the meeting of the American Medical Association in Chicago, in June, and appeared in *The Journal*

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since at least the 16th century. It is difficult to decide, however, as to the identity of the pneumonia with what was described by contemporary writers in those long past epidemics, since they usually limited themselves to the mention of a few symptoms followed by a lengthy discussion of their treatment of the cases. Few performed autopsies or recorded descriptions that can be recognized. Nevertheless, their writings suggest that in many of the epidemics they must have been dealing with the same condition that has existed during the past winter.

In the 16th century there were many epidemics throughout Italy, beginning in 1535 and sweeping over the whole peninsula. In Switzerland it was known as the malignant stitch, or *Alpenstich*, and by 1576 it had spread over Western Europe.

The attack began with a chill, pain in the head and chest, and a cough which was at first dry but afterwards attended with expectoration. The patient became delirious or fell into a stupor; loose evacuations followed, and death occurred on the 6th or 7th day, or if the disease was protracted over the 9th day the prognosis was good. Massa described pleural effusions, and Coiter states that in all the cases which he described he found the lungs filled with putrid blood, turgid, and indurated, while Dodonæus writes that abscesses were frequent in the lungs. In the 17th century there were similar epidemics, and several authors report finding serous and blood-stained effusions in the pleura and pericardium, and the lungs in part condensed, in part rendered diffluent by suppuration. In the 18th century, according to Hirsch, there were still epidemics of the same "typhoid pneumonic" character in Spain, England, Italy, Switzerland, France, and North America. In all these the malignant type of the disease is emphasized and the hepatization or purulent softening of the lungs is

of the American Medical Association (MacCallum, W. G., *J. Am. Med. Assn.*, 1918, lxxi, 704).

My grateful acknowledgment is due to the men who worked on these Commissions, for their aid, and to the various members of the staffs of the Base Hospitals at these two places. Especially are my thanks due to Major L. Clendening, of Fort Sam Houston, who furnished clinical data of most of the cases, and to Major Joseph L. Miller, of Camp Dodge, who did the same for the cases studied there. Major D. Glomset, who was in charge of the laboratory at Camp Dodge, also afforded us every aid in his power.

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given as the characteristic anatomical feature. Morgagni describes the lungs as firmly hepatized. The disease prevailed widely in France in the latter part of this century. De Sauvages in 1790 describes peripneumonia typhodes, and Deplaigne an epidemic among soldiers at Valenciennes. They made postmortem examinations and found suppurative processes in the lungs with effusion of pus or gelatinous serum in the chest and sometimes in the pericardium. There were pleural adhesions too, but the other organs were normal except for swelling of the liver. In Great Britain and in Germany there were also severe epidemics.

In North America there were, as described by Webster, epidemics in Connecticut in 1712, 1719, 1760, and 1795. Bard tells briefly of a similar epidemic at Huntington, Long Island, in 1749, and recounts symptoms resembling those which we have seen recently, but he made no dissections. I have not been able to associate these epidemics with the gathering of troops during the Revolutionary War or to find any papers referring especially to this period.

In 1812, however, there began a great epidemic which, starting in Canada, spread throughout the Northern States and finally into the South. There is a great deal of literature about this, and the *Medical Repository* and the *American Medical and Philosophical Register* made a special point of gathering together communications and essays relating to it. There is also a book by James Mann, Hospital Surgeon of the Army, published in 1816 (Medical Sketches of the Campaigns of 1812, 1813, and 1814) which gives a good description of the condition, including a few postmortem observations. From these it may be learned that some of the soldiers died with extensive pleural effusion, sometimes of thick pus, as in the case of one man whose pleura was drained by an incision between the ribs, and sometimes of a thick yellowish whey-colored fluid, while a membrane of coagulated lymph lined the cavity of the thorax. In one case the lungs were dark purple, but on incision thick pus could be forced by compression out of the air cells. In another the lungs were contracted, compact, tough, and almost destitute of air vessels. Another showed the lung large, hard, and adherent to the upper part of the cavity. It appeared like the liver, tender and easily lacerated with the fingers, and entirely destitute of the spongy texture peculiar to healthy lungs. In its superior part

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adjoining the clavicle and near the trachea was a large sphacelus, part of which had been coughed up. Pus was by compression squeezed out of the air cells. In another case the lung was adherent on all sides, and specks of pus were found throughout it, but no abscesses.

Still another case presented a lung in which a small portion had come to resemble the liver, and the cells contained pus. The other lung exuded pus on every incision. It was not much dissimilar to a honeycomb, if filled with pus. The last, or eleventh case revealed three pints of limpid glutinous serum resembling whey in each cavity of the thorax. The right lung was contracted to half its natural size. The upper part was consolidated and hardened, feeling and appearing like a piece of heart boiled. Adhesions had formed to the spine, ribs, clavicle, and pericardium. The lobe was so much drawn to the spine that no adhesion existed between it and the ribs of the anterior part of the thorax. In the upper part of the lobe immediately under the clavicle there was an abscess as large as a goose egg. There were found adhering to the pleura and lungs a membrane of coagulated lymph and some similar thick pieces resembling what is commonly called mother of vinegar. The left lobe appeared little diseased, but on cutting into the substance drops of pus were squeezed out of its cells. While one or two of these cases appear to have been instances of lobar pneumonia, the others in which there was such extensive pleurisy and from the lungs of which drops of pus could be squeezed resemble closely the cases found in the present day epidemic.

The descriptions of the clinical symptoms given by Mann, Bard, Eights, Matson Smith, Valentine Mott, McBride, and others agree closely, but by far the best is given by James Low who described the beginning of the epidemic in Albany in October, 1812.

"The onset is with a chill, prostration and a feeble pulse, horror and distress from pain in the head, back, and extremities. The tongue is furred, the breathing insupportably laborious even when the pain in the chest is not severe, and every muscle concerned in this function ceases to act until goaded on by volition. When the pain is acute the anguish is inexpressible. Every cell in the lung seems infarcted and weighed down by the load.

"Restlessness, distressing dreams, sudden frights, and starting from sleep attend most cases. Many are unable to endure the horizontal posture from a sense of suffocation which attends that position. Coma and delirium ferox are frequent symptoms and there are aphthæ and ulcers in the throat in some cases.

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The disease sometimes terminates in scarlet fever, measles, or an anomalous rash, all of which prevailed, as was the case in other countries where the same epidemic has raged. Morgagni, Coiterus, and Wierus describe the same in Italy and Germany, Cleghorn in Minorca, Sydenham, Huxham, and Home in England."

Low saw gangrene of the leg in one case. Hosack also mentions autopsies in this epidemic in which he found an overloaded state of the vessels of the lungs. A large effusion of serum and sometimes purulent matter and the adhesions between membranes covering the lungs and those lining the chest show that there has been inflammation of the lungs. It was, he decides, a local inflammation with a typhous state of the whole system from which he refers to it as peripneumonia typhodes.

Mann, in another paper written from Plattsburg, states that the most prevalent disease was measles, which predisposed those who had it to pneumonia. He gave once more a description of the lungs which were inflamed with adhesions to circumjacent parts, with the surface covered with yellowish gelatinous semiputrid extravasation. The spongy texture of the lungs was lost and the organ assumed the compactness of the liver.

McReynolds in describing an epidemic among troops at Black Rock gives similar details of autopsies, and so does Hudson concerning an epidemic on the Niagara Front. Hudson was especially interested in the extension of inflammation through the diaphragm to the surface of the liver. A similar affection with pleurisy with serous effusion and pulmonary changes was observed in the New York Hospital in January, 1813.

After the disease had raged among the troops and inhabitants of northern New York it appears to have occurred with especial intensity in Dutchess County, East Chester, and West Chester, as well as in New York City and Long Island, but there were also many cases in Connecticut, Vermont, and Maine. Nowhere are the pulmonary changes minutely described, but it is evident from the occasional clear descriptions of definite hepatizations and the vague descripition in other cases of congestion alternating with abscesses or with a form of consolidation from which one could squeeze pus from the bronchi that most of it perhaps was not definite lobar pneumonia but probably a form of bronchopneumonia with extensive pleural exudate. It

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died out in these states in 1815, but passed into the Southern States and persisted until 1826.

Although there were many epidemics in various parts of Europe at this time I have not been able to learn so far that this type of disease was prominent in the armies engaged in the Napoleonic Wars.

From 1815 to 1862 there were occasional epidemics. Little information appears to be available regarding the troops during the Civil War. Bartholow described the occurrence of measles and its sequelæ in the camps, and Woodward gives statistical information showing that measles was prevalent, that pneumonia followed it, and that the mortality was considerable, but these conditions were greatly overshadowed by the colossal prevalence of typhoid fever and dysenteric disease, and Woodward's attention seems never really to have reached pneumonia. The following is abstracted from this history.

Measles.—During the years covered by statistics there were 67,763 cases of measles, with 4,246 deaths among white troops, with a mortality of 6.27 per cent. Most of this mortality was due to secondary pulmonary affections. Many deaths were referred to pneumonia without mentioning measles. Per 1,000 the average annual rate was 30.41, the maximum 77.57 in the 1st year, the minimum 1.98 during the last year. Many regiments suffered at recruiting stations.

In colored troops there were 8,555 cases, with 931 deaths, or 10.88 per cent of fatal cases.

In the Confederate Army of the Potomac there were 8,617 cases in an army of 58,360 during July, August, and September, 1861, 430 cases in October, 241 in November, 79 in December, 34 in January, 1862, and 8 in February. A succession of epidemic waves involved susceptible men of successive additions to strength of command.

As the new men came within the influence of the contagious focus the disease spread, giving a sudden elevation to the line of prevalence which thereafter fell until fresh additions occurred with a corresponding rise in its level.

Among the white troops the line of prevalence shows a seasonal influence as well as that due to the aggregation of susceptible individuals. The warm season operated favorably on these troops. The disease was especially severe among negroes, being characterized by bronchial inflammation, pneumonic congestion, and solidification, laryngeal congestion and edema, and sometimes affections of the intestinal mucous membrane.

Clinical records of measles show a return to duty 3 or 4 weeks after onset, but in many cases the stay in the hospital was prolonged for as many months by the continuance of bronchial inflammation or the supervention of bronchopneumonia or diarrhea. In some cases the specific agency manifested its virulence

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by a dark purple color of the eruption and symptoms of internal congestion. In general the point of interest is the consecutive disease. Sometimes pneumonic congestion was suddenly developed by exposure while the skin was affected, but more frequently pulmonary disorders, including consumption, appeared to be engrafted on the patient during convalescence. Laryngitis in some cases caused sudden death, and in others a temporary or even permanent aphonia. Cerebral meningitis sometimes occurred, and intercurrent or sequent attacks of erysipelas were common. Conjunctivitis was a frequent sequel and deafness followed the invasion of the middle ear by way of the Eustachian tube. Occasionally the ear became involved in the suppuration of the glands in its neighborhood. Edema of the feet, orchitis, and ischiorectal abscess including fistula *in ano* were among the sequelæ.

"Recruits from the city are more likely to have passed through the disease in childhood than those from the rural districts. City regiments are therefore to be preferred in this connection. When the call to service is urgent this becomes a secondary matter. The liability to disease under exposure to its causes must be accepted as a part of the danger to be faced. Measles will thus continue to be a subject of interest and anxiety to army medical men until the discovery of a means of protection against it independent of subjection to its influence in previous epidemics."

Later (page 788) he suggests the propriety of inoculation.

Pneumonia.—"61,202 cases of pneumonia occurred among the white troops during the war, with 14,738 deaths, so that the importance of pneumonia as a destroyer of life in our camps and hospitals can hardly be overestimated. The postmortem records of cases reported as pneumonia show that death in the majority of instances resulted not alone from hyperemic or inflammatory processes in the pulmonary tissues, but from these in conjunction with similar processes affecting particularly the pleural membranes, bronchial tubes, and pericardium. With the production of these congestive or inflammatory results the malarial, typhous, and tuberculous cachexias and the specific cause of measles were apparently often connected."

Of 435 cases recorded after postmortem examination, 300 were distinguished as lobar pneumonia, 135 as secondary or catarrhal inflammation. Of the 135 cases, 101 were associated with measles. These cases are inadequately described and as a rule it is merely stated that parts of the lung were hepatized, and in a few instances thickening with softening of the bronchi was mentioned. Pleurisy with effusion was common and there is slight mention of laryngitis. Pericarditis was present in a few cases but was by no means so frequently associated with secondary pneumonia as with the acute lobar cases. Pleurisy as such seems to have been recorded in 31,852 cases during the war, but although 590 were fatal only 45 were observed and described post mortem and of these 6 were connected with measles.

Of the cases of bronchopneumonia following measles the lungs of three have been preserved in the Army Medical Museum in

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Washington, and Dr. Lamb was kind enough to allow me to study them and even to take portions for microscopic study. They are from Case 50 (Medical and Surgical History of the War of the Rebellion, Vol. I, Part 3, Medical Volume, page 789), Case 105 (page 794), and Case 134 (page 798). All these cases were observed by Surgeon E. Bentley, U. S. Volunteers, Third Division Hospital, Alexandria, Virginia.

The history in Case 50 states that Private J. B. Talbot, aged 23, was admitted Feb. 13, 1864, with pleuropneumonia following measles and died Feb. 29. Postmortem examination showed that the lower lobe of the right lung was hepatized, red, and presented on section a number of small superficial abscesses. The pleura was thickened (Specimen 345, now renumbered 7,792). The lung is covered with fibrinous exudate and most of it is spongy in texture, but it contains some distinct firm nodules which are branched at times.

Section of this lung no longer stains well, but the outlines of cells may be discerned. There is in the section a patch of consolidation and then one of air-containing tissue with two small foci of consolidation. These have central bronchioles which contain exudate and have lost their epithelium. The walls are very thick and infiltrated with mononuclear cells and are penetrated by many blood vessels distended with blood. The adjacent alveolar walls are similarly infiltrated and contain dense plugs of fibrin with desquamated epithelium.

The larger area of consolidation shows several bronchi with the same change. The walls of a rather large one are especially infiltrated. The more peripheral alveoli have dense contents of fibrin and epithelium. In the more central part of the patch the tissue is disintegrated and full of very small broken cells, possibly leucocytes. There is a mass of granular material at one spot resembling bacteria.

With Weigert's method the bacteria stain quite sharply and great masses of definite streptococci are found in the midst of the necrotic area. No other organisms were found.

This appears to have been a case of streptococcal bronchopneumonia in which certain areas of consolidated tissue have become necrotic in mass and contain large clumps of bacteria.

The history of Case 105 is as follows: Private Jacob Maust, aged 20, was admitted Mar. 26, 1864, moribund from pneumonia after measles. He died on the 28th.

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On postmortem examination it was found that the left pleural cavity contained a pint of serum and the lung was coated with thin pasty lymph, the lower lobe being partly hepatized.

Specimen 343, now numbered 7,790, shows the following. The pleura is greatly thickened and edematous with wide interlobular septa. The lymphatics are enormously wide and are distended with cell masses. In these and on the surface of the pleura there are large numbers of streptococci in distinct chains which stain well. No influenza bacilli could be demonstrated. The bronchi are distinctly thickened. New blood vessels in great numbers have formed in their walls, the epithelium is lost, and streptococci occur in their purulent contents. There is collapse, but not much consolidation about them.

This appears to be a case of interstitial bronchopneumonia with lymphatic transportation of the streptococci.

The history of Case 134 is as follows: Private John H. McMichael, aged 19, was admitted Mar. 11, 1864, with pleurisy and laryngitis, secondary to measles. He died on the 23rd.

On postmortem examination the larynx and trachea were found to be inflamed and filled with tenacious mucus; right lung collapsed and friable. Lower lobe thickly coated with pseudomembrane. Left lung slightly congested (Specimen 342, now numbered 7,789).

The lung shows a thin layer of fibrin; the pleural surface and the pleura itself are markedly thickened. Interlobular septa are prominent. At the base of the upper lobe there is a small area of diffuse consolidation. The rest is air-containing except for numerous small nodules of consolidation with central bronchioles.

Sections show numerous small bronchi filled with debris of leucocytes. The epithelium is desquamated and the underlying tissue necrotic. The alveoli round about are filled with fibrin and cells, some of which are leucocytes. There is no great interstitial change in most of the lung. Definite cocci in pairs and short chains are found in the bronchioles. In other places bronchial and blood vessel walls are markedly infiltrated with cells. The intervening lung substance is air-containing.

This is a focal streptococcal pneumonia in which there is little interstitial change but chiefly small peribronchial foci of lobular pneumonia.

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It is evident that in these three cases we have representatives of the types of streptococcal pneumonic lesion which occur in the epidemic of today. The first case is one of interstitial bronchopneumonia with large areas of necrosis, the second belongs to the same type but without the necroses, while the third is an earlier stage with much less interstitial change. It is especially interesting that after 54 years in alcohol the streptococci still stain brilliantly.

Surgeon Ira Russell also reported that there had been 784 cases of pneumonia at Benton Barracks, Mo., in 1864, of which 156 died. Beside these there were 675 cases of measles, of which 130 died of pneumonia. He distinguishes congestion, typhoid, and pleuropneumonia. There is a marked difference in the morbid appearance of the lungs in the pneumonia following measles from their appearance in pneumonia produced by other causes. Hepatization is less marked, the lung tissue oftener edematous or filled with serosanguineous fluid and containing a sufficient quantity of air to make it float on water. When pressed between the fingers a large quantity of bloody serum exudes. The lung frequently passed from this edematous condition, without going through the stages of red and grey hepatization, into that of purulent infiltration.

Since the Civil War other epidemics of pneumonia have been described, but it is generally difficult from the clinical descriptions to determine the nature of the disease, and practically none of the authors in this country appear to have recorded postmortem examinations.

In Europe many such epidemics were briefly described also (Laveran, Bard), without adding perceptibly to the comprehension of the disease. But with Bartels there began a more accurate anatomical study of the peculiar form of bronchopneumonia which follows measles, whooping cough, diphtheria, and perhaps other acute infectious diseases.

Delafield in various publications in this country has given clear descriptions of the peculiarities of this form of bronchopneumonia in children and in adults, emphasizing its interstitial character and the lateral involvement of the alveoli which adjoin the bronchioles together with the accompanying atelectasis. His understanding of the contrast between this type of pulmonary affection and the sort of

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exudative process which follows the aspiration of infected materials into the bronchi, or the other examples of terminal patchy pneumonia characterized by the filling of the alveoli which are connected with the infected bronchioles with an exudate of polymorphonuclear leucocytes, is satisfactory and his descriptions form a model of conciseness. At this time there was a prevalent doctrine which distinguished between croupous or lobar pneumonia in which there is an exudate of leucocytes and fibrin, and catarrhal or bronchopneumonia in which fibrin was less in evidence and the alveoli contained large mononuclear cells mixed with others. This seems to be an inadequate basis for the anatomical distinction, and more recent writers have not accepted it, although these terms are still used.

Since Bartels' paper, a series of German publications has appeared, describing more clearly the interstitial form of bronchopneumonia in children after diphtheria, measles, and whooping cough, and from an anatomical point of view these leave little to be desired, although none except those of Dürck and Finkler are concerned with the bacteriology of the disease. From these are derived no doubt the description found in most of the text-books, although the description given by Orth is evidently from his own observations. Wagner, Jürgensen, Aufrecht, Kromayer, Koester, Wygodzinski, Dürck, Honl, Steinhaus, Hart, Jochmann and Moltrecht, and Hecht have all contributed papers which are easily accessible.

These papers agree closely in their descriptions of the pathological anatomy of this form of bronchopneumonia, the best of which are those of Steinhaus and Hecht. Wygodzinski distinguishes lobular and confluent forms in which the alveoli are filled with a fibrinous and leucocytic exudate, from peribronchitic inflammation, but he also recognizes combinations. Honl points out the resemblance of the small firm nodular consolidation in these lungs to miliary tubercles, but insists that tuberculosis is not of frequent occurrence after measles, and that the common impression that it is, may depend upon the erroneous interpretation of these peribronchial nodules as tubercles. He saw the peculiar epithelial giant cells upon which later writers have laid stress.

Steinhaus reviews the earlier German literature, gives a clear description of the pulmonary lesions, and summarizes his paper as follows:

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Measles pneumonia is in the beginning not a lobular inflammation but appears in minute foci, of which several are found in a lobule. It is never catarrhal, since fibrin is abundantly present.

The focal consolidations result from a primary bronchiolitis and peribronchiolitis through a propagation of the inflammatory irritant by way of the lymph vessels. There are several types of lesions. (*a*) The acute focus with exudation into the alveoli. This may arise by extension of the inflammation from the bronchioles to adjacent alveoli which do not belong to its respiratory district or by propagation along its lumen to its own alveoli. In the zone of fresher exudate fibrin is always present. (*b*) The more chronic focus, proceeding in the form of an interstitial peribronchitis with advanced changes in the interstitial tissue but no exudation in the alveoli.

This change appears to be related in its origin to the peribronchial and perivascular lymph follicles. The interstitial change arises very early in measles pneumonia and distinguishes it from the croupous form. The distinction between the acute and the more chronic foci of pneumonia lies in the presence of a leucocytic infiltration in the first, a lymphatic infiltration in the second. He apparently saw no giant cells, but Hecht who also studied the lungs of children lays especial stress on their presence in his paper which has the title "The giant cell pneumonia of children." This is a form of pneumonia which occurs only in young children after measles and whooping cough in connection with a hypertrophic bronchitis. The giant cells arise from the epithelium either by incomplete division or by coalescence. They could never be produced experimentally in rabbits by intrabronchial injections of staphylococci or pneumococci, but could be imitated closely in animals injected intratracheally with various metallic salts (especially silver nitrate and copper sulphate) or ammonia. Karsner and Meyers described and discussed a similar case in a child and reference will be made to this later in connection with one of our cases.

All these papers have dealt with children and I have found little referring to such bronchopneumonia in adults. Delafield recognized it in adults, but his attention was chiefly directed to the disease in children.

Mathers describes an epidemic of pneumonia occurring in Chicago during the season 1915–16 in which he isolated *Streptococcus pyogenes* in a majority of instances. His description of the lung refers to

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the gross appearance only. There were extensive pleuritis and pericarditis and the cut surface of the lung was smooth and mottled greyish red and dark red. The greyish areas varied in size and consistency, some being firm and dry while others were moist and viscid. They had no relation to bronchi and were sharply outlined like infarcts. Other dark red areas were soft and hemorrhagic. The description is too indefinite to allow one to recognize the condition with certainty.

During the present war, epidemics have been studied in the north of France by Hammond, Rolland and Shore, and at Aldershot in England by Abrahams, Hallows, Eyre, and French. They describe a purulent bronchitis which is fatal and from which they isolated the influenza bacillus from the sputum in most of the cases. They found other organisms at times, including the pneumococcus, streptococcus (five times), *D. catarrhalis*, staphylococcus, *M. tetragenus*, etc. Pleurisy appears not to have been common and mention is made of only eight cases in which a clear yellow fluid had accumulated in the pleural cavity. The bronchi are filled with pus and there is a peribronchiolitis. Photographs of sections of the lungs show the peribronchial infiltration distinctly, and the anatomical description which is given with these makes it seem evident that the lesion is practically the same as that which we are about to describe for the epidemic in this country. The lack of pleurisy is one great point upon which they differ from our cases, and the second is in the predominant rôle of the influenza bacilli.

In a letter dated June 22, 1918, from a hospital in France, Dr. Archibald Malloch writes me concerning such an epidemic in which he had studied nine cases at autopsy. He says nothing of empyema in these cases.

"Clinically the cases were generally like capillary bronchitis, and as a rule no dulness could be made out, although sometimes this was present. There were marked dyspnea and cyanosis. At autopsy there was often no consolidation of any extent but grey-white pus was found even down to the finest bronchioles (swarming with *B. influenzæ* and there obtained in pure culture). At other times there were small areas of atelectasis with tiny yellowish abscesses in them. On the other hand, some of the lungs showed confluent bronchopneumonia. Two of these cases showed an endocarditis with vegetations, from the cultures of which Major Rhea grew *B. influenzæ* in pure culture."

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II. THE EPIDEMIC IN THE UNITED STATES ARMY CAMPS.

The conditions existing in these ancient epidemics have in a sense been repeated on a magnified scale in the course of the assembling of the troops from all parts of the United States in the present war, and the results with respect to disease of the respiratory organs have been much the same. It is obvious that the sanitary conditions surrounding the cantonments and camps have been extremely good as far as forms of disease which were especially destructive in the Civil War and in many other wars are concerned, and the result is that with the aid of vaccination against typhoid fever, paratyphoid, and smallpox, those diseases have not appeared. Even diphtheria is now practically under complete control. But sanitation and preventive medicine are as yet helpless against measles and pneumonia, and therefore these diseases have swept through the well ordered camps as they did in 1812.

The draft brought together large numbers of men of ages from 21 to 31 years from all conditions of life. Many of them had lived in cities, accustomed all through their lives to close intercourse with the densest populations and these had passed through all the ordinary diseases of childhood and had acquired immunity. Others, however, and especially perhaps those from the South, had lived in remote rural districts under entirely different conditions with but little contact with any great number of other people. These came to the camps unprotected from any disease except smallpox and typhoid fever. The compulsory vaccination conferred this protection and eliminated these diseases from the army in a way which could not be paralleled by any measures of sanitation which aimed at their exclusion by even the most rigid control of all the recognized channels of infection.

To the remaining acute exanthematic diseases and to respiratory infections these men were highly susceptible. To other infections they were also susceptible, but these have assumed such a prominent place in the history of disease in the camps that the rest appear rather insignificant.

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It must not be stated that the respiratory diseases occurred exclusively in the troops of rural origin, since they gained such virulence as to affect all, but it does seem clear that immunity acquired by exposure and infection in early life has played a great part in protecting the men of some of the camps from disease.

Emphasis should be laid, I think, upon the importance of measles in the inception of this epidemic. Measles has prevailed to an extraordinary degree in many of the camps in the South, and there too have arisen the greatest epidemics of bronchopneumonia. When pneumonia taken as a whole and including lobar and all forms of bronchopneumonia is plotted out on a map, as was done in the office of the Surgeon General, so as to show the camps in which the greatest number of cases occurred, as black circles, and especially when the position of these camps is indicated according to the district from which they drew their troops, all the black circles are in the South. Any such statement is necessarily somewhat inaccurate. Measles is not absent in the northern camps nor is pneumonia. Lobar pneumonia caused by the pneumococcus, which no one suspects of being especially a sequel of measles, probably occurs in much the same proportion throughout all the camps. But the form of bronchopneumonia which has for years been recognized as a common sequel of measles has appeared in enormous proportions in the southern camps in which hundreds and even thousands of cases of measles developed. It is true that this type of pneumonia in these camps frequently occurred in patients who had not had measles, and it is clear that it is due to some second infection and not to the measles itself. It was not altogether surprising, therefore, to find large epidemics of the same type of bronchopneumonia arising later in northern camps where measles had not existed to a great degree and in troops which had not been in contact with the few cases of measles which were isolated in distant barracks.

Briefly stated, the great epidemic seems to be an epidemic of bronchopneumonia, with measles as the most important predisposing cause, but the bronchopneumonia, which itself is due to a secondary infection, later arose independently of measles in individual cases and in other camps when the agent which caused the secondary infection became virulent enough to give rise to the disease independently.

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The following study of the forms of pneumonia which prevailed makes no attempt to outline the extent of these diseases in the various camps, since that information will be available from the reports of the office of the Surgeon General. Nor is it intended to trace the course of the various epidemics or to give statistics of the incidence of pneumonia or the number of deaths caused by it. Instead it is an attempt to analyze the character of the respiratory diseases observed at Fort Sam Houston, Texas, during February and March, and at Camp Dodge, Iowa, during May, from the standpoint of the student of their etiology and pathological anatomy.

In the study of the respiratory disease in these camps a consistent plan was followed. In a large number of cases observed clinically, cultures were made from the sputum, swabs from throat, and cultures from the circulating blood and fluid aspirated from the pleural cavities. These were, of course, of great importance in diagnosis and threw much light upon the condition found at autopsy. The most satisfactory information was derived, however, from the cases in which the bacteriological results could be confirmed and controlled by cultures from the tissues at autopsy, and in as far as these cases were concerned we endeavored to tabulate the records in such a way as to show at once the results of cultures made during life and after death from all these sources. It was interesting to find that repeated cultures made during life and after death sometimes showed the disappearance of one organism and its replacement or overgrowth by another. Our information is sufficiently complete for this purpose in about 49 cases of pneumonia which are therefore given in Table I. The cases which were studied clinically only need not be included, since they have been discussed in other papers.

It will be seen from this table that a great variety of lesions and several types of infection are represented here with various combinations. In general, analysis of the cases shows that there were two main forms of infection, that in which the pneumococcus was the etiological agent and that in which this part was played by *Streptococcus hæmolyticus*.

The influenza bacillus was frequently found in the sputum and occasionally in the lungs and pleural fluid. It was always associated with the streptococcus, however, and it is difficult to assign it a pre-

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Autopsy No.
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dominant part in the causation of the pneumonia. In general the pneumococcus of whatever type produced lobar pneumonia, and the streptococcus either what we shall describe as interstitial bronchopneumonia, or another lesion to which for convenience we assign the name lobular pneumonia.[1] The exact biological nature of this streptococcus and its identity in different camps are still subjects which are actively discussed. It seems to be the same wherever it has been found, but it will require time to determine whether there are several strains at work. Indeed, from many camps there come reports of numerous cases due to a non-hemolytic streptococcus. All these important points must be settled by further study, which must also decide the significance of the influenza bacillus, staphylococcus, and other organisms in the production of the disease. Our own experience has led us to believe that a fairly constant hemolytic streptococcus is the important factor.

In practically all the cases of streptococcus infection there appears, if there is sufficient time before death, a serofibrinous or fibrinopurulent pleurisy. This sometimes persists as an empyema even after the earlier pulmonary lesions from which it originated have completely or almost completely disappeared. All possible combinations of these forms of pneumonia occur, and it has therefore seemed best to consider all the cases in six groups into which they readily fall as follows: (1) interstitial bronchopneumonia; (2) interstitial bronchopneumonia with lobular pneumonia; (3) lobular pneumonia; (4) lobar pneumonia; (5) lobar with interstitial bronchopneumonia; (6) old empyemas.

It is, of course, possible that lobar and lobular pneumonia may occur together, but I do not think that we have met with this combination.

Cases 14 to 58 were studied at Fort Sam Houston, Texas, Cases 165 to 205 at Camp Dodge, Iowa.

[1] It has been pointed out by various writers that the term lobular pneumonia should be applied to a consolidation involving a lobule, but such accurate limitation does not take place. On the other hand, it is difficult to find any other convenient term which will designate a patchy consolidation in which the alveoli are filled with an inflammatory exudate of leucocytes and fibrin. Such an exudate is similar to that which when diffusely distributed over a whole lobe constitutes a lobar consolidation, and it seems permissible to employ the term as a conventional name for this condition.

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1. Interstitial Bronchopneumonia.

Case 14.—J. McL., age 22 yrs. Entered hospital Jan. 1, 1918, with typical measles. Discharged Jan. 10. Second entry Jan. 16. Has not felt well since leaving hospital, still coughs, has a fever and headaches. *Diagnosis.*—Acute bronchitis until Jan. 22, when he became worse and was transferred to the pneumonia ward delirious, very ill, and coughing. Signs of consolidation in right lower lobe and râles over left lower lobe. Inspiration difficult. Marked cyanosis. Leucocytes 16,000. Temperature ranges from 99–104° F., pulse 100–150, respiration 20–55. Died Feb. 2. Autopsy Feb. 2.

Anatomical Diagnosis: Bilateral interstitial bronchopneumonia with hemorrhage and atelectasis; serofibrinous pleuritis (right).

Left pleural cavity.—There is no excess of fluid. Pleural surfaces smooth. No adhesions. *Right pleural cavity.*—The cavity contains about 1,000 cc. of slightly turbid brownish fluid with floating shreds of fibrin. Pleural surfaces covered with thick, shaggy, yellow exudate of fibrin. Lymph glands in the mediastinum enlarged. *Left lung.*—Surface is smooth. The lung is voluminous, but the lower part of the upper lobe and the lower and posterior portions of the lower are collapsed and pasty. Insufflation distends most of the upper lobe and part of the lower. On section some of the bronchi of the upper lobe stand open and are conspicuous as empty, thick walled grey tubes. They are surrounded by areas of hemorrhage. In the lower lobe all the bronchi appear as thick walled tubes with opaque yellow contents and are surrounded by hemorrhagic areas which become confluent. In the larger bronchi the deeply congested mucosa is covered by a thin opaque grey film. The bronchial glands are not greatly enlarged. *Right lung.*—Greatly compressed by the pleural effusion. It is covered by a layer of fibrin which varies from 2 mm. to 2 cm. in thickness. The lymph glands at the hilum are greatly enlarged. All the lobes of the lung are completely collapsed, but the upper lobe and the anterior portions of the lower lobes may be distended by insufflation. In the lower and posterior portions of the lower lobe there are numerous firm grey areas each of which shows a central bronchus and a surrounding zone of hemorrhage. These foci become confluent in places or stand out separately so that several may be seen in each of the lobules of the lung. The lobules are sharply outlined by the interlobular septa which are edematous and therefore conspicuous.

Cultures failed to grow through an accident. Smears from the lung showed Gram-positive cocci in chains.

Microscopic Examination.—The left lung contains air and most of the alveoli are unchanged, but many of the smaller bronchioles are filled with an exudate of polymorphonuclear leucocytes among which a few streptococci are found. The epithelium of such bronchioles is in places intact, in other places broken and partly desquamated (Fig. 1). The wall is greatly thickened and its connective tissue and smooth muscle elements are spread apart by red corpuscles and mono-

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nuclear wandering cells of various types. Wherever lymphatics are visible in these walls they contain red corpuscles and mononuclear cells. The adjacent alveoli are filled with blood, desquamated epithelial cells, and mononuclear wandering cells together with a few polymorphonuclear leucocytes. The alveolar walls are infiltrated with mononuclear cells and thickened. Both bronchi and alveoli contain networks of fibrin. The alveoli which open directly into the bronchi contain leucocytes in greatest abundance; those which lie adjacent to the wall of the affected bronchioles appear to contain blood and mononuclear cells rather than leucocytes. Organization of the exudate in the bronchi is found in an early stage in some places (Fig. 2).

The right lung shows a more advanced change. The pleura is covered with fibrin upon the surface of which streptococci are found. The pleura itself is densely infiltrated with blood. It is markedly thickened by the formation of a vascular granulation tissue which has not destroyed all the remnant of the pleural lining cells. The whole framework of the lung has become conspicuous through the widening of the interlobular septa, peribronchial and perivascular tissues, and the alveolar walls themselves by the most extensive infiltration of mononuclear wandering cells. The lung is partly collapsed, but the enormously thick walls of bronchi and alveoli are very distinct. It is especially in the neighborhood of the infiltrated bronchi, interlobular septa, and pleura that the alveolar walls are distended with cells. In the walls of blood vessels and bronchi and in the interlobular septa lymphatics are easily seen. Most of them are thrombosed and contain streptococci as well as lymphocytes and fibrin coagulum. The more distant alveoli contain only masses of desquamated epithelial cells. Those nearer the bronchioles and participating in the formation of the peribronchial consolidation are filled with dense fibrin together with the cellular elements described. In this firm fibrin as well as in the bronchioles there is already visible a rather extensive growth of connective tissue. Definite strands of vascularized tissue are seen in the lumen of some bronchi. In one there is a mass of such tissue covered completely by a continuous growth of bronchial epithelium. The mediastinal lymph glands are swollen, their marginal sinuses filled with large mononuclear cells among which are many streptococci. These are entangled in a dense fibrin network.

The other organs show nothing abnormal.

This is a typical case of interstitial bronchopneumonia following measles and showing on one side empyema, collapse, peribronchial nodules with great interstitial infiltration, thickening of pleura and septa, and advanced organization of bronchial and intraalveolar exudate.

Case 15.—B. H., age 19 yrs. No history of measles. Since Jan. 3, 1918, cough and expectoration with pain in chest and fever. Entered hospital Jan. 14. No rash, no sore throat. Dulness and râles over whole right lung. Râles but no dulness over left. Leucocytes 16,800. Temperature 100–104° F., pulse 100–150, respiration 30–60. Died Feb. 1. Autopsy Feb. 2.

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Anatomical Diagnosis: Bilateral interstitial bronchopneumonia with fibrinopurulent pleuritis.

Left pleural cavity.—Contains very little fluid. The surfaces are covered with a thin exudate of fibrin which glues them together. *Right pleural cavity.*—Contains about 1,500 cc. of turbid khaki-colored fluid with floating shreds of fibrin. The lung is adherent in its upper posterior aspect; the lower lobe is collapsed and flattened. *Left lung.*—In both upper and lower lobes there are collapsed areas, those in the lower lobe occupying the whole lower and posterior portion. In the upper lobe there are a few bronchi filled with yellow plugs, especially in the collapsed area. In the lower lobe these are much more numerous and toward the hilum they are thickened and embedded in yellowish opaque areas. There is no definite hemorrhage about them. The larger bronchi are deeply congested. *Right lung.*—The pleura is thickened and covered with a dense layer of yellow fibrin. The lung is completely collapsed and flabby. It is studded throughout with yellowish areas of consolidated tissue in the center of which there is generally to be seen the ragged lumen of a bronchus. Such areas vary from 2 to 7 mm. in diameter, but in the lower lobe they become confluent, in one place to form a mass 3 cm. in diameter. They are surrounded by grey atelectatic lung substance. The bronchi are distinctly dilated toward the periphery of the lung. Bronchial and peritracheal glands much enlarged.

Microscopic Examination.—The left lung shows the bronchioles throughout their extent filled with a debris of epithelial cells, red corpuscles, and great numbers of leucocytes among which streptococci are found in pairs and chains. Gram-negative bacilli, apparently influenza bacilli, are also present. The epithelium is greatly desquamated. The walls are thickened partly by the great distension of the small blood vessels and the separation of the connective tissue fibers, but chiefly by the infiltration of mononuclear cells. The lymphatics are distended and contain mononuclear cells, red corpuscles, and streptococci. The surrounding alveoli contain a few leucocytes, red corpuscles, desquamated epithelial cells, and fibrin. Mononuclear cells are also present. There is much coagulated fluid in these alveoli. There are also a few areas in which the alveoli are packed with polymorphonuclear leucocytes with little fibrin. In these areas streptococci are found, although they are rare in the alveoli which contain mononuclear and epithelial cells.

The right lung is much more extensively altered as though by a process of longer standing. The pleura is converted into a thick granulation tissue with blood vessels growing straight up into the hyaline fibrin. The bronchi are dilated, filled with leucocytes and disintegrated epithelium. The epithelial lining is largely destroyed and the walls are very greatly thickened and converted into a sort of vascular granulation tissue densely infiltrated with mononuclear cells. For some distance round each bronchus the alveolar walls are greatly thickened by the infiltrating mononuclear cells (Fig. 3). Elastic tissue stains show that the framework of the alveolar wall is spread apart by these cells. The alveolar con-

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tents are composed of dense fibrin with desquamated epithelial and mononuclear cells. Much of this exudate has undergone complete organization or replacement by new vascular connective tissue which extends from the bronchi into many alveoli. This gives added density to the consolidated areas. The walls of the blood vessels are spread apart and thickened through the infiltration of their adventitial coats. The interlobular septa are greatly widened by infiltration with fluid and cellular exudate and apparently also by the new formation of connective tissue. However, lymphatics appear in the walls of the bronchi and of the blood vessels and in these interlobular septa they are very wide and filled with a coagulum of fibrin with blood corpuscles, leucocytes, and especially mononuclear cells. These fibrin plugs are densely sown with streptococci which are to be found there in enormous numbers even though search through the lung tissue elsewhere fails to reveal them. This tends to support the view that they are in this way transmitted to the pleura.

Bacteriological cultures revealed *Streptococcus hæmolyticus* in the heart's blood and lung.

This is a typical case of interstitial bronchopneumonia with empyema. There is interstitial new formation and organization and streptococci show well in the lymphatics. There is great thickening of alveolar walls and great density of the exudate. In places there is lobular pneumonia.

Case 16.—J. W., age 18 yrs. Entered hospital Jan. 24, 1918, with painful cough which began 10 days previously. Had a chill 4 days ago. No history of measles. On entry lungs showed dulness and râles in the right back, otherwise clear. Leucocytes 22,200. Temperature 99–104° F., pulse 120–150, respiration 30–50. Died Feb. 2. Autopsy Feb. 2.

Anatomical Diagnosis: Bilateral interstitial bronchopneumonia with fibrinopurulent pleuritis and pericarditis.

Left pleural cavity.—The lung is bound to the pleura by fresh fibrinous adhesions. There is no fluid exudate. *Right pleural cavity.*—The surfaces are hemorrhagic and covered with a thick layer of fibrin which binds them together anteriorly. In the posterior part of the cavity there is an accumulation of yellow turbid fluid. Between the upper and lower lobes behind the midlobe there is an enclosed pocket filled with this turbid exudate (Fig. 4). *Pericardial cavity.*—Contains 500 cc. of turbid fluid. The surfaces are covered with a thick shaggy layer of fibrin. *Left lung.*—The upper lobe is greatly distended with air and the bronchioles are normal except in the lower part where they become the centers of small grey nodules surrounded by hemorrhage. The lower lobe is completely collapsed, and on section dark purple in color but studded with small grey nodules about 2 mm. in diameter which in places become confluent. *Right lung.*—The bronchial glands are much enlarged, the lung is very bulky and heavy and covered with thick fibrinopurulent exudate. Most of the lung except the apical portion is collapsed. The smaller bronchi are grey and thickened, especially in the lower lobe where they form innumerable small grey nodules, several to each

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lobule. The interlobular septa are prominent and grey. *Liver.*—Surface smooth and mottled, lobules large and very distinct with grey margins and dark red centers.

Microscopic Examination.—The right lung is most extensively affected, practically all the alveolar walls being much thickened by the mononuclear infiltration. The changes in this lung are thus not exclusively in the bronchi. The pleura is thickened by a vascular granulation tissue over which lies the fibrinous exudate. This is best seen in the interlobar space where the fibrin loses its staining power where the bacteria become most abundant. Streptococci are present in great numbers in certain rarefied areas and there many of them are enclosed in phagocytes so that they look like little balls of organisms. The interlobular septa are much thickened both by edema and new formation of connective tissue cells and by infiltration of mononuclear cells. The lymphatics are often greatly distended and thrombosed and loaded with streptococci. The bronchi are filled with leucocytes among which streptococci may be found. Many have lost their epithelium. In others the bronchial epithelium is lifted up by a rich granulation tissue which has developed beneath it. In all, the wall is greatly thickened and very vascular and densely infiltrated with mononuclear cells. The alveoli in the neighborhood but also throughout rather wide areas of the lung substance contain much free blood. This hemorrhage is widespread. They also contain dense fibrin, desquamated epithelial cells, and mononuclear cells, but in many places this type of exudate is replaced by newly formed connective tissue which is richly vascular and which runs from one alveolus to another. In the alveoli which enclose the denser masses of fibrin no bacteria are found. There are, however, a few alveoli which contain polymorphonuclear leucocytes and these are full of streptococci. In the bronchi the exudate is frequently replaced by long branching cylinders of fresh vascular connective tissue. These may stretch from one wall of the bronchus to the other (Fig. 5). The infiltration of the whole framework of the lung with mononuclear cells and its general thickening through new formation of connective tissue cells are a striking feature.

The bronchial lymph glands are swollen and hyperemic, their peripheral lymph sinuses are full of large phagocytic cells, and often plugged by a fibrin network. Bacteria are present, but not in great numbers and not in phagocytes.

The liver shows extensive fresh focal necroses mostly in a midzonal position. They are irregular in form and extent. All the liver cells remain in position as red necrotic cords, and leucocytes are packed among them.

The pericardium shows a rather fresh fibrinopurulent exudate without any organization. The layer of lining cells is still intact.

Cultures from the heart's blood, lungs, and pericardial exudate showed *Streptococcus hæmolyticus.*

This is a typical case of interstitial bronchopneumonia with empyema and pericarditis with exceptional infiltration and induration without very extensive or marked peribronchial consolidation. Bacteria numerous in lymphatics.

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Case 32.—R. S., age 25 yrs. Patient had a cold with cough dating from Dec. 15, 1917. Illness began with measles about Feb. 2, 1918; entered another hospital Feb. 4. Transferred to this hospital Feb. 7. Still shows a fading macular eruption and marked conjunctivitis. Throat injected and covered with whitish membrane in patches. Dulness at the bases of both lungs behind. Breathing not distinctly tubular. Râles over the whole lung. Temperature 99.6° F., pulse 120, respiration 32–34. Very restless and delirious. Died Feb. 9, 1918, 4.25 a.m. Sputum showed influenza bacilli and a few streptococci. Culture from circulating blood gave no growth. Autopsy Feb. 9, 1918.

Anatomical Diagnosis: Clinical history of measles. Bilateral interstitial bronchopneumonia. Subacute fibrinous pleuritis.

Left pleural cavity.—The cavity contains a little yellowish fluid, about 150 cc. At the apex of the lung are a few fibrous adhesions and denser ones exist between the lower lobe and diaphragm. The pleura over the posterior surface of the lung is dark greyish red and roughened by exudate. *Right pleural cavity.*—Largely obliterated by old adhesions especially in the lower part. There is no accumulation of fluid and no fresh fibrinous exudate, but the surface is covered by a pleura thickened to the consistency of stiff kid leather. *Left lung.*—The lung is voluminous and in general distended with air except for one area of collapse in the lower lobe. On section it is studded throughout with minute nodular areas of consolidation which project like tubercles. The bronchi are somewhat reddened, the bronchial glands moderately enlarged. *Right lung.*—This lung is insufflated with air in all three lobes. The upper lobe shows some atelectatic patches which are firmer than the remainder of the lobe. These are 2 cm. in diameter. On section there are found scattered over the whole cut surface of the upper and lower lobes small grey nodules 1 to 2 mm. in diameter which resemble miliary tubercles. On close examination many of these nodules have a central depression which appears to be the lumen of a bronchiole. Many of them are pale yellowish grey with a surrounding paler grey zone. A few are surrounded by distinctly collapsed areas. There are lobules in which a dozen or more of these nodules are visible on the cut surface and in which hyperemia with some hemorrhage makes them stand out prominently. In the more insufflated areas they are less conspicuous and it seems possible that the thin grey halo may be due to collapse or obliteration of the immediately adjacent alveoli. The bronchi are reddened but not dilated.

Epiglottis, uvula, larynx, and trachea show no especial abnormality, although the lymph glands about the larynx are enlarged.

Microscopic Examination.—The pleural surface of the right lung shows a dense vascular fibrous tissue beneath which is a looser tissue. There is a strand or two of fibrin in its most superficial part. The interlobar space is obliterated by similar tissue.

The bronchi are only slightly altered (Fig. 6). They are in their smaller branches filled with leucocytes among which a few streptococci can be found. No influenza bacilli can be found in the sections. The epithelium is irregularly

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interrupted, and in some cases extensively desquamated. In places leucocytes have accumulated beneath it. The walls of these bronchi and bronchioles are infiltrated with cells among which there are a few leucocytes. Most of the cells, however, are mononuclear wandering cells of the type of lymphocytes, a few plasma cells, and cells of somewhat larger size with paler nucleus. The adjacent alveolar walls are similarly distended and thickened with mononuclear cells. The epithelium of the alveoli is partly desquamated. The alveoli contain leucocytes in the areas round the terminations of the bronchi but there is very little hemorrhage. Also there is very little fibrin and there are no solid plugs such as are seen in more advanced cases. There is, however, coagulated fluid which fills the alveoli round the minute areas of consolidation. There are a few rather more extensive patches of consolidation in which for some distance the alveoli are filled with leucocytes, ragged networks of fibrin, blood, and coagulated fluid, but these too are distinguished by the marked infiltration of the bronchial and alveolar walls and the walls of the blood vessels with mononuclear cells (Fig. 7). Apart from these the alveoli are filled with air and have thin, delicate walls until the pleura or larger blood vessels are approached. There the thickening of the walls again appears. The interlobular septa are not very conspicuous and microscopically are not much infiltrated. Lymphatics can be injected from the pleura, and although they contain some small plugs of fibrin and cells, the injection is fairly complete. The mucosa of the trachea is much inflamed and infiltrated with mononuclears. There are a few streptococci upon its surface. The tonsils show many streptococci in their crypts.

Cultures from both lungs showed *Streptococcus hæmolyticus* and the influenza bacillus.

Case 34.—J. W. G., age 18 yrs. Said to have had measles at the age of 7. Began to feel ill on Jan. 27, 1918, with coryza, conjunctivitis, sore throat, malaise, and fever, but no chills. On Feb. 1 measles rash appeared and the patient entered the hospital with a bad cough and abundant sputum. There was difficulty in breathing, insomnia, and delirium. Pharynx reddened, old Koplik spots on buccal mucous membrane, dark purplish papular crescentic rash on face, neck, chest, arms, and back. This later became confluent in places and assumed a purpuric appearance. The rash began to fade on Feb. 5, but could be seen also in the mouth. Breathing difficult especially on inspiration when accessory muscles are brought into play. No definite localized dulness in the thorax nor any tubular breathing; moist râles heard everywhere. Feb. 6, (Dr. Cole) respiratory movements slight, breathing almost entirely diaphragmatic. Marked retraction of lower chest on inspiration. Percussion note resonant over both sides anteriorly and posteriorly. On auscultation, inspiration is loud and accompanied everywhere by numerous coarse and medium mucous râles, but expiration is practically not heard. Examination reveals no areas of definite impairment or blowing breathing. Leucocytes 28,000. Temperature 100–104°F., pulse 100–140, respiration 25–50. Died Feb. 10 at 2.30 a.m., 14 days after onset of measles. Culture of sputum shows *Streptococcus hæmolyticus*. Autopsy Feb. 10.

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Anatomical Diagnosis: Bilateral interstitial bronchopneumonia with fibrinopurulent pleuritis.

Left pleural cavity.—Contains a moderate quantity of fluid which is turbid and yellowish with a little floating fibrin. The pleura over the lung is distinctly thickened and white. *Right pleural cavity.*—Contains no excess of fluid. The surfaces are smooth and glistening except over the posterior and diaphragmatic surfaces where the gloss is lost. *Left lung.*—There are no adhesions although the pleura is thickened and dull looking. The posterior and lower part of the upper lobe is dense and on section it is found that in this region, which extends about 4 cm. inward from the pleura, the interlobular septa are greatly thickened and stand out prominently as greyish yellow ridges. The bronchi are very much thickened and are filled with purulent exudate. In each of the sharply outlined lobules there are several focal consolidations which correspond with the terminal branches of the bronchi. The surrounding lung tissue is greyish yellow, edematous, and rather translucent. The uppermost part of the lung is air-containing (Figs. 8 and 9). *Right lung.*—The lung is voluminous and its surface is smooth except over the base of the lower lobe where there is a thin fibrinous exudate. In the upper lobe the interlobular septa are prominent and there are a few projecting nodules which correspond to the bronchial branches. The bronchi are very much thickened although the surrounding lung substance appears to be air-containing. The lower part of the lower lobe shows the same marking out of the lobules and thickening of the bronchi with small peribronchial areas of consolidation. The upper portion and anterior parts of all the lobes are air-containing. The bronchial glands are much enlarged.

Other organs appear normal.

Microscopic Examination.—The lungs show the most advanced changes. The pleura over the left lung is thickened so as to form a layer of dense granulation tissue upon the surface of which there is a thin interrupted layer of very compact fibrin. The lymphatics in the pleura are not especially conspicuous. The interlobular septa are very wide, as was observed in the gross specimen and are the seat of a great quantity of fluid and a network of fibrin. There are streptococci scattered in the meshes of this fibrin in small numbers. This edema and infiltration of the interlobular septa is not universal. In places the septa while greatly thickened are quite dense and composed of new connective tissue. The most striking feature of the sections is the presence of enormous lymphatics which lie in the course of these interlobular septa or in one margin of the septum (Fig. 10). They form broad beaded canals often 2 mm. in width, each segment adjoining the next by a truncated end across which the septum can be seen. These compress the adjacent alveoli. The endothelial lining can be seen clearly in places. They are filled with leucocytes, fibrin, and coagulated fluid, and mingled with these are enormous numbers of streptococci in rather long chains.

The bronchi are altered in extreme degree (Fig. 11). Few of them retain their epithelial lining in anything like its normal arrangement. In some it is com-

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pletely desquamated, in others lifted up as a whole and collapsed together (Fig. 12). In still others it is stretched out so that the cells are much flattened. Some of the bronchi show a high columnar epithelium which appears to form a layer several cells deep. The lumen of the bronchus is filled with leucocytes or a mixture of leucocytes, red corpuscles, and desquamated epithelium with many streptococci, but no other organisms. The walls are greatly thickened and extremely vascular. Many new vessels must have been formed, and there are evidently many newly formed connective tissue cells. The wall is thus composed of a loose vascular tissue which is densely infiltrated with mononuclear cells of various types. None of these is ever very large, however. The same is true of the alveolar walls in a decreasing degree as one passes from the bronchus, large vessel, interlobular septa, or pleura into the lung substance. Nevertheless there are many areas in which the alveolar walls are thickened and infiltrated over a wide extent of tissue. In the alveoli near the affected bronchi there are desquamated epithelial cells and mononuclear wandering cells together with a dense mass of fibrin. In many places this fibrin is distinctly invaded by new connective tissue cells and in places even by blood vessels. The organization is nowhere complete, however. The fibrin tends to decrease as one passes from the bronchus, and the more outlying alveoli are filled with fluid and red corpuscles. These together with the degenerated and desquamated epithelial cells probably give the yellowish color to the wide zones surrounding the affected bronchi. There are, however, in connection with some of these bronchi considerable areas of alveoli which are packed with leucocytes held in a delicate network of fibrin and heavily loaded with streptococci. The organisms in these patches are as numerous as one ever sees pneumococci and are enclosed in phagocytes in the same way. That they are streptococci is seen from their occurrence in long wavy chains, although most of them are in pairs or short chains. The blood vessels are not markedly affected. Thus in this case the advanced stages of the interstitial bronchopneumonia are pretty well developed in association with patches of a more distinctly lobular pneumonia, extensive collateral edema, and great distension of the lymphatics. The enormous filling of the lymphatics with streptococci seems to afford the best explanation of their transportation to the pleura. It is evident that the lymph stream is stopped and that they must extend by their own growth.

The bronchial gland is densely infiltrated with large mononuclear cells so that its architecture is almost obliterated. It is very hyperemic and contains enormous numbers of streptococci in the sinuses.

Case 37.—A. H., age 24 yrs. Had pneumonia in 1914 when he underwent an operation for resection of a rib for empyema. For several days prior to Jan. 28, 1918, had a cold. On that day felt sick, aching all over, chill with fever and vomiting. Entered hospital Jan. 29. Examination Feb. 11 showed extreme respiratory difficulty with cyanosis. Measles rash over whole body. Conjunctivitis. Inspiration seems especially difficult and cyanosis is out of proportion

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to the signs in the chest. No definite dulness or tubular breathing anywhere. Large moist râles over the entire chest. Patient remained in same condition extremely sick until Feb. 13 when he died, 16 days after the onset of measles. Sputum was yellow, mucopurulent, and contained influenza bacillus and *Streptococcus hæmolyticus*. Blood culture taken Feb. 11 was negative. Autopsy Feb. 13, 1918, 1 hour after death.

Anatomical Diagnosis: Clinical history of measles. Bilateral interstitial bronchopneumonia with fibrinopurulent pleuritis.

Left pleural cavity.—Contains 500 cc. of turbid fluid with thick floating shreds of fibrin; between the lung and the pericardium there are slight adhesions. *Right pleural cavity.*—Obliterated by firm adhesions. There is a scar in the posterior axillary line on the right side over the 9th rib, part of which was removed in the old empyema operation. The two ends of the rib are connected by fibrous tissue, and spicules of bone have grown out into this portion which evidently contained periosteum. *Left lung.*—The lung is not very voluminous, the lower lobe being partly collapsed. The upper lobe is air-containing throughout, the apex and anterior border being especially distended. At the upper posterior tip of the lower lobe there is a firm area. *Right lung* (*Fig. 13*).—Voluminous and in general air-containing. There are, however, some collapsed patches in which one can feel nodules. On section the lung is found to be studded throughout with small greyish nodules which project in groups of two or three. One can readily see with the naked eye that they are the branches of the bronchioles with greatly thickened opaque yellowish white walls and central lumen. Some of them are surrounded by zones of collapse, others by a halo of dark greyish red. The bronchi when opened are grey, not especially reddened or distended with exudate. The bronchial glands are enlarged. Trachea and main bronchi are somewhat reddened.

Cultures at autopsy from the blood gave no growth. From the right lung *Streptococcus hæmolyticus* and the influenza bacillus were recovered.

Microscopic Examination.—The left lung shows a pleura slightly thickened and composed of edematous new tissue covered with a dense layer of fibrin. The bronchi are dilated and are quite large even near the pleura. The epithelium is stretched out into thin flat cells. They contain leucocytes with very few streptococci in chains but great numbers of influenza bacilli. The walls of the bronchi are extraordinarily thick. They are loose in texture as though spread out by edema. The original tissue can no longer be recognized but is replaced by the lattice work of new fibers among which there are many mononuclear wandering cells. The adjacent alveolar walls are distinctly widened by the infiltration of such mononuclears, but they are not very thick. The alveoli contain dense networks of fibrin, many desquamated epithelial cells, and some mononuclears. In places there are alveoli filled with leucocytes. The interlobular septa are not conspicuous, and lymphatics are hardly to be found. The blood vessels are practically unchanged in appearance. Such a portion of

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the lung appears solid because of the confluence of the areas of consolidation from one bronchiole to another.

In the right lung the striking feature is that the alveolar tissue between the bronchi is air-containing and made up of very thin walled alveoli. The pleura is thickened, but the thickening is produced by many frayed out layers of old fibrous tissue which formerly bound the lung to the chest wall. There is no fibrin. The interlobular septa are thick, dense, and fibrous without much evidence of recent inflammatory change. The bronchi are greatly altered, and contain in most cases a mass of leucocytes, but the epithelial lining is usually intact, at least in part. The wall is very thick and dense and is somewhat infiltrated with mononuclear cells. In many cases the great thickening of the bronchial wall is all that attracts attention because the adjacent alveoli are normal. In other places the epithelium is partly desquamated; the surrounding alveoli are filled with organizing dense fibrin and mononuclear cells (Fig. 14). The organization of the fibrin appears to begin in, or extend into the bronchi, for the exudate is often found partly replaced by new connective tissue. There are in other places still patches of alveoli directly associated with an affected bronchus which are filled with leucocytes or fibrin. These give the character of lobular pneumonia, or would if they were extensive or numerous enough.

The dense old thickening of pleura, interlobular septa, and bronchial walls, in contrast with the changes in the opposite lung, suggests that these more chronic or finished changes may have dated from the time of his previous empyema with operation. Nevertheless most of the small peribronchial foci of infiltration in this lung which project like tubercles over the whole surface are undoubtedly the result of the present infection.

Case 39.—C. L. A., age 19 yrs. Had whooping cough when a baby, measles at the age of 9, diphtheria at 12, and mumps and scarlet fever at 14. Began on Jan. 23, 1918, with a chill, fever, headache, and nosebleed. No conjunctivitis, coryza, or sore throat. Has had no rash at any time, although on his transfer card was the diagnosis measles. Entered hospital Jan. 25 with cough and shortness of breath, with pain over left chest and left side of abdomen. Is extremely sick, cyanotic, and cold. Breathing shallow and rapid. Clear mentally. Eyes bright with no conjunctival hemorrhages. Physical examination of the chest shows shifting flatness on the left side with tympany in the axilla and a definite splash on shaking. Breath sounds over the tympanitic front are amphoric. On the right side there is dulness over the lower back. Breath sounds distant; expiration is indistinct. Numerous moist and sonorous râles. Heart is greatly displaced to the right. On Feb. 13 aspiration of the left chest yielded a thin purulent fluid which in films and cultures showed *Streptococcus hæmolyticus* in pure culture. Sputum foul, greyish white, purulent, and tenacious. Contains *Streptococcus hæmolyticus* and *B. influenzæ*. Blood culture negative. Died Feb. 14, 1918, 4 a.m. Autopsy Feb. 14, 1918, 10 a.m.

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Anatomical Diagnosis: Doubtful clinical history of measles. Bilateral interstitial bronchopneumonia with fibrinopurulent pleuritis and pneumothorax (left).

Left pleural cavity.—Contains air. There are also 1,500 cc. of thin turbid brownish fluid with very little floating fibrin. The sediment settles leaving the fluid almost clear. *Right pleural cavity.*—Contains no excess of fluid. Pleural surfaces anteriorly smooth and glistening, but over the posterior part of the lung they have lost their gloss. *Left lung.*—The lung is small and heavy and appears to be entirely collapsed. The pleura over it is grey, slightly thickened, and studded here and there with hemorrhages over its slightly roughened surface. The uppermost part of the upper lobe can be distended with air, but the lower and posterior parts remain collapsed. The bronchi are dilated and thickened and the small branches are surrounded by a grey-yellow zone which is solid. The upper part of the lower lobe can be distended. The lower part is solid, but it can be seen easily that each tiny branch of the bronchi is thickened and surrounded by its own yellowish solid nodule and there it is the confluence of these nodules which gives the solidity to the whole. In the lowermost edge there is even a portion which can be distended with air although most of the bronchioles are packed with exudate. The bronchi are widened and their walls thickened there also, and one has the sensation of cutting a rubber tube when they are opened with scissors. *Right lung* (*Fig. 15*).—The lung is voluminous and shows a smooth pleural surface. When distended with air it is found that a patch in the upper lobe at the lower margin and one in the lower lobe above the middle remain dense and nodular. Each bronchiole on section is thickened and yellow and surrounded with a little zone of consolidation and a wider zone of hemorrhage. The large bronchi are reddened, but the lung otherwise seems normal.

Cultures at autopsy from the pleural fluid, pericardial fluid, blood, and both lungs show *Streptococcus hæmolyticus.*

Microscopic Examination.—The lesion in the left lung is rather more advanced than in the right, but of the same character. The pleura is thickened, but interlobular septa are not greatly widened. The bronchi in the left lung have in many instances retained their epithelium, although the wall is greatly thickened and infiltrated. Hemorrhage is common in this wall and in the adjoining tissue. The infiltration and thickening of the alveolar walls extend quite wide of the bronchi. In places there is complete loss of the epithelium, and a bronchus except for its orderly arrangement of blood vessels in the wall would resemble an abscess. Very few streptococci are visible even in the bronchi. The surrounding tissue is consolidated not only by the interstitial thickening of the alveolar walls, but by the alveolar exudate which is composed partly of fibrin, blood, and epithelial cells, and is partly already organized into a loose connective tissue. Hemorrhage is abundant in the alveoli and in the tissues. There are several areas where the alveoli are filled with an exudate of polymorphonuclear leucocytes. These are somewhat richer in bacteria.

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Case 41.—P. A. I., age 20 yrs. Began Jan. 28, 1918, with chill, fever, and cough. Rash appeared Jan. 31, but there was no conjunctivitis or coryza. Admitted to hospital Feb. 2. Sweats profusely, complains of difficulty in breathing, and coughs a great deal. There is marked cyanosis, patient half sitting up in bed and bringing into play the accessory muscles of respiration. Face flushed, rash well marked over the body. Pharynx very red. Dulness over left axilla and lower back and in right interscapular region. Breathing distinct but not tubular. Numerous sonorous râles. Left chest aspirated Feb. 13, but no fluid obtained. Sputum grey and purulent and tenacious; contains *Streptococcus hæmolyticus* as predominating organism. Blood cultures made on Feb. 13 and 14 when patient was dying gave pure culture of *Streptococcus hæmolyticus*. Died Feb. 14, 1918, 17 days after the onset of measles. Autopsy Feb. 14, 1918.

Anatomical Diagnosis: Clinical history of measles. Bilateral interstitial bronchopneumonia with serofibrinous pleuritis.

Left pleural cavity.—Contains about 300 cc. of turbid fluid with shreds of fibrin. The pleural surface of the upper lobe of the lung is smooth, while that over the posterior part and lower lobe is roughened by fibrin. *Right pleural cavity.*—Contains about 500 cc. of turbid fluid. The surfaces are roughened by fibrin. *Left lung.*—The bronchial lymph glands are very soft and large. The bronchi contain a greyish mucoid material. The upper lobe of the lung is pale and air-containing, the lower lobe partly airless and dark red. On section the upper lobe is studded with small yellowish grey nodules 2 to 3 cm. in diameter with a central lumen. These are prominent, but when the lung has been hardened and freshly cut they appear as small branching bronchi with thickened walls and opaque purulent contents. In the lower lobe the bronchi are thick, dark red, and prominent, and stand open. The nodules surrounding the small ones are larger than in the upper lobe, granular, yellowish grey and red, and confluent. Alveolar contents can be seen to project in these nodules. On longitudinal section of the bronchi the yellow opaque contents contrast with the thick grey wall and the outer zone of hemorrhages followed by the grey granular consolidation. The walls of these bronchi in the smaller branches are 1 mm. thick (Fig. 16). *Right lung.*—The anterior portions of the lobes are air-containing, while the posterior parts are dark red, heavy, and airless. The upper lobe can be partly insufflated. It is studded with yellowish grey peribronchial nodules. Interlobular septa broad and conspicuous. In the posterior part the lung becomes solid, the peribronchial nodules are large, 1 to 2 cm. in diameter, and of a uniform yellow color (Fig. 17). They have a ragged central bronchial lumen and are separated from neighboring consolidations by a deeply hemorrhagic solid lung substance. This contrast between bright yellow nodules of homogeneous consistency and the deep red intervening areas is very striking and gives a peculiar marbling not seen in other cases. Nevertheless this is only an exaggeration of the conditions found in other lungs. The lower lobe is firm and densely studded with rather large peribronchial nodules about the smaller

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bronchi. It is the smaller branches of the bronchi whose walls become greatly thickened. One finds on passing to the larger ones that their walls are practically unaffected. Bronchial glands are large and soft.

Cultures from the blood, lungs, and pericardial fluid showed *Streptococcus hæmolyticus* in pure culture.

Microscopic Examination.—The same general condition is found throughout both lungs. It is the interstitial bronchopneumonia described so often, but developed to its maximum. The pleura is not greatly thickened, but is covered by a thin layer of dense fibrin in most places. The interlobular septa are wide and contain large lymphatic channels choked and distended with masses of cells and fibrin. Many of these cells are polymorphonuclear leucocytes, while others are mononuclear cells.

The bronchi are dilated, often to such an extent as to reduce their lining epithelium to a flattened layer throughout. It is probable that this is not a mere effect of stretching, but is caused in part by this. The lumen is full of leucocytes with relatively few streptococci. These organisms do not in this case penetrate into the tissue in any great numbers and are scarcely to be found in the alveoli, although they are found in the distended lymphatics. No other bacteria are found. The wall of the bronchus is sometimes colossally thickened (Fig. 18) and forms a dense mass of mononuclear wandering cells embedded in a meshwork which is composed of the original connective tissue and muscle of the bronchus. But to this there has evidently been added a great deal of new connective tissue which is extremely vascular, especially just beneath the epithelium (Fig. 19). Possibly this great vascularity represents only the extreme hyperemia of the preexisting tissue. One might regard this as the result of enormous hyperplasia of the minimal supply of lymphoid tissue which exists in the normal bronchial wall. Possibly that is a correct interpretation for some of it, since in other less advanced cases it is sometimes seen that the lymphoid tissue is much increased in bulk, and even becomes continuous to form a mantle about the bronchus. Occasionally these bronchi are surrounded by air-containing tissue whose alveolar walls are then almost normal. But usually they are surrounded by a considerable area of lung tissue consolidated by the filling of the alveoli with blood, desquamated epithelial cells, and fibrin, together with a few mononuclear cells (Fig. 20). In such areas the alveolar walls are greatly thickened by mononuclear invading cells, and this is especially true of the tissue about blood vessels and septa. The appearance is similar to that seen in other cases except that everything is exaggerated in this case.

The large dense yellowish white areas described in the upper lobe of the right lung represent the extreme of this exaggeration. They have central bronchi and are made up of tissue whose framework is densely infiltrated but whose alveoli are filled with solid masses of fibrin enclosing very few cells. There are no leucocytes and only a few remnants of epithelial or mononuclear cells. Blood has ceased to exist in these alveoli, but there is a beginning organization of the fibrin.

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In the periphery of such areas red blood corpuscles become very numerous in the alveoli and still farther out are the predominant elements. It gives the impression that red corpuscles were at one time present in the alveoli which are now so densely filled with fibrin. The blood vessels in these lungs are not altered except by the great infiltration of their walls with mononuclear cells, and in the larger ones by the thrombosis of their adventitial lymphatics. They are never thrombosed.

Case 49.—C. P., age 21 yrs. No previous history of exanthematic disease. On Feb. 9 vomited, after which he began to have fever. Next day noticed a faint redness over the skin of the chest. Entered hospital Feb. 11 with a bright red rash over chest, neck, face, abdomen, and arms. Diagnosis of scarlet fever was made. Feb. 18, the urine showed a faint trace of albumin, no casts. Became restless and delirious. Dulness with râles over upper and midlobes of right lung. Died Feb. 21, 1918. Autopsy Feb. 21, 1918, at 2 p.m.

Anatomical Diagnosis: Clinical history of scarlatina. Interstitial bronchopneumonia with empyema (right). Bilateral lobular pneumonia.

Left pleural cavity.—Contains no excess of fluid. Surfaces of the pleura smooth and glistening. *Right pleural cavity.*—The lower lobe of the right lung is adherent by fibrinous adhesions to the costal pleura and diaphragm. The anterior margin of the lung is adherent to the pericardium by light fibrinous adhesions. Between the lower lobe and the pericardium there is a pocket containing about 75 cc. of greenish yellow turbid fluid with shreds of fibrin. The upper lobe is collapsed and between it and the chest wall there is an accumulation of slightly turbid greenish fluid in which there are large floating shreds of fibrin. The surface of all the lobes is covered by a fibrinous exudate which in places measures 3 mm. in thickness. *Left lung.*—The surface is smooth and the lung is in general air-containing and easily inflated. In the anterior portion of the lower lobe there are several small areas in which the alveoli are filled with an exudate of greyish red color. There are also a few bronchi which show a thickened wall and are surrounded by a hemorrhagic zone. *Right lung.*—The lung is small and collapsed with a thickened pleura. The lobes are bound together and covered by a thick yellow coat of fibrin. The upper lobe is air-containing in its apical portion but in the lower part the bronchi are thickened and surrounded by greyish zones of consolidation which tend to become confluent. The intervening lung substance is grey and rather translucent. The lower lobe is uniformly studded in its posterior portion with thickened bronchioles with grey confluent halos partly separated by a darker grey-red intervening lung substance. The interlobular septa are wide and prominent. The bronchial lymph glands are large and softened. *Kidneys.*—No gross abnormality.

Cultures from pleural fluid, right lung, and heart's blood all show *Streptococcus hæmolyticus.*

Microscopic Examination.—The right lung shows a thickened pleura with granulation tissue covered with fibrin. The interlobular septa are wide and infiltrated

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with fluid, fibrin, and mononuclear cells. The lymphatics are not very conspicuous. The bronchi contain leucocytes and show desquamation of epithelium with thickening, infiltration, and hyperemia of the wall. The adjacent and even quite far distant alveoli present similar infiltration and thickening of their walls. They contain much fluid with desquamated epithelial cells or are filled with dense fibrin. Organization of this exudate has occurred in places. There are a few areas in which the alveoli are filled with an exudate of leucocytes and fibrin, but these are not so numerous as might be expected from the gross appearance. This is essentially an interstitial bronchopneumonia following scarlatina, with very few foci of lobular pneumonia. The sections show few streptococci but contain large bacilli resembling *B. subtilis* and many Gram-negative bacilli which appear to be *B. influenzæ*.

Case 167.—W. J. H., age 27 yrs. Began with scarlet fever on Mar. 18, 1918, and after recovery from that developed measles on Apr. 11. On Apr. 21 suffered from severe pain in chest. Aspiration of the right pleura gave a turbid fluid which contained *Streptococcus hæmolyticus*. The diagnosis of lobar pneumonia with consolidation of the right lower lobe was made on Apr. 22, and confirmed by x-ray. Empyema on the right side was recognized on May 1, and the patient died on May 4, at 6.15 p.m. Cultures at autopsy were contaminated, but the blood showed *Staphylococcus aureus*, the left lung and right pleura a non-hemolytic streptococcus. Autopsy May 5, 1918.

Anatomical Diagnosis: Interstitial bronchopneumonia with abscess formation. Empyema (right).

There are two needle puncture wounds in the midaxillary line on the right side, one over the 6th, the other over the 7th interspace. *Left pleural cavity.*—Contains no fluid. Surfaces smooth and glistening. *Right pleural cavity.*—The anterior portions of the pleural cavity are free from adhesions and the surfaces are smooth. Posteriorly there are adhesions which can be easily broken through and there is then found behind the posterior part of the lower lobe a cavity thickly lined with fibrinous exudate and containing about 50 cc. of turbid brownish fluid. The lower part of the lower lobe is adherent. *Left lung.*—Air-containing throughout except for a few obsolete tubercles. *Right lung.*—The anterior portions of the upper and lower lobe and the whole of the middle lobe are air-containing. The posterior part of the upper lobe is solid; the area of consolidation measuring about 4 cm. in diameter is, on section, grey, smooth, and elastic, with thickened pleura. Over the flabby, heavy posterior part of the lower lobe there are large irregular areas where the pleura is smooth and glistening but apparently necrotic. These areas are easily broken through, disclosing ragged confluent cavities half filled with soft shreddy necrotic lung substance. On section much of this lobe is collapsed without definite consolidation, but the cavities are formed in a greyish red, smooth, and elastic area of consolidation. They are crossed by bridges containing large blood vessels and are sharply outlined by a yellowish necrotic layer. A bronchus entering one of these cavities loses its wall abruptly.

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Microscopic Examination.—The consolidated portion of the right lung shows a great deal of thickening and infiltration of the alveolar walls, of the bronchi, and of the interlobular septa. In places the interstitial thickening of the tissue especially of the alveolar walls is great and there is much infiltration of polymorphonuclear leucocytes in addition to the mononuclear wandering cells. Many of the alveoli are reduced to very small cavities lined with high cubical epithelium or filled with desquamated epithelium. There is widespread organization of the exudate. There are also some rather small patches of lobular pneumonia with the alveoli filled with leucocytes. The cavities are formed, however, independently of these in the more indurated tissue in which there is chiefly desquamation of epithelium. Their walls are made up of a layer of vascular granulation tissue lined with necrotic material and fibrin. In other places there is no such granulation tissue and merely the sudden cessation of the dense lung tissue and its replacement by coagulated necrotic material. This is loaded with chains of streptococci, but no other organisms are seen.

Case 171.—C. S., age 28 yrs. Had no predisposing disease. No history of recent measles. Began suddenly on Apr. 21, 1918, with a pain in his chest. The diagnosis of lobar pneumonia involving the right lower lobe was made upon entrance into the hospital and confirmed by x-ray. The diagnosis of empyema was made later and a resection for drainage was performed on Apr. 24. The pleural fluid gave a culture of *Streptococcus hæmolyticus*. Died May 5, 1918. Autopsy May 6, 1918.

Anatomical Diagnosis: Interstitial bronchopneumonia (right). Empyema (bilateral). Acute nephritis.

Left pleural cavity.—Contains about 350 cc. of reddish brown liquid with floating flakes of fibrin. The surfaces posteriorly are deep red in color and covered with fresh shaggy fibrin. *Right pleural cavity.*—In the right back 4 cm. below the angle of the scapula and in the line of the 10th rib there is a wound 6 cm. long which extends into the pleura. The right lung is displaced far upward, the lower lobe being adherent behind between the 2nd and 3rd ribs. The apical part of the lung is densely adherent. The pleural cavity extends about the back of the lung as high as the second rib and is widely open below the lung. Its surfaces are covered with a thick yellow fibrinous exudate. *Left lung.*—The posterior portions of the upper lobe and most of the lower lobe are collapsed but can be inflated easily. There are no areas of consolidation. The smaller bronchi are slightly reddened and contain sticky mucus in the lower lobe but they are not thickened. *Right lung.*—The lung is completely airless except for a small part of the upper lobe. The lower part of the upper lobe feels firm, the lower lobe flabby and soft. On section it is found that the lower part of the upper lobe is uniformly consolidated through an area about 5 cm. in diameter. The middle lobe can be completely inflated. The lower lobe presents in its posterior part some bronchi with purulent contents which are surrounded by irregular grey patches of consolidation. The remainder of the lung

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is smooth and satiny on section but quite collapsed. *Kidneys.*—Alike and measure about 12 by 6 by 3.5 cm. They look rather swollen. The capsule strips off smoothly leaving a greyish surface. On section the cortex measures 7 cm. in thickness. It is pale and the labyrinthine portions of the striations are opaque and yellow but straight. The glomeruli are visible as pale dots.

Cultures at autopsy from the right lung and both pleural cavities showed *Streptococcus hæmolyticus.*

Microscopic Examination.—The consolidated portion of the upper lobe of the right lung is found to be covered with a thick exudate of fibrin which overlies a vascular granulation tissue. This tissue becomes very wide and edematous at one point where it extends over the lung and connects with a broad interlobular septum. Blood vessels are numerous in this tissue and the lymphatics are wide but not thrombosed. The bronchi are very wide, their lining layer thrown up into many folds. The epithelium is preserved and as a rule the lumen is filled with leucocytes among which are streptococci. The walls are moderately thickened, hyperemic, and infiltrated with mononuclears. The lung substance is in large part collapsed. The alveolar walls are not greatly infiltrated or thickened but contain desquamated epithelial cells and fluid. There is nowhere any exudate of leucocytes and nowhere much fibrin, although a little is to be seen here and there. There are many alveoli in one part which contain strands of a hyaline compact fibrin. In other sections the thickened bronchi are conspicuous in a less atelectatic lung tissue.

The kidney shows in general a cloudy swelling of the epithelium. The glomeruli are often rather enlarged and show capillaries distended with leucocytes and blood, these elements being also found in the tubules. There is much interstitial infiltration of the tissue with mononuclear cells and leucocytes in patches which occur in both cortex and the outer zone of the pyramid.

In this case the lung is compressed by the pleural effusion, but itself shows relatively little pneumonic alteration. Nevertheless there is a distinct infection of the bronchi and a characteristic alteration of their walls.

Case 174.—G. R., age 28 yrs. No history of measles or other predisposing disease. Began gradually on Apr. 5, 1918, with a pain in the chest and cough. On Apr. 8 diagnosis of lobar pneumonia involving right lower lobe was made. Radiograph on Apr. 12 showed involvement also of the right upper lobe with possible accumulation of fluid in the pleural cavity. This was confirmed by aspiration on the same day and the patient was referred to the surgeon for operation. The 8th rib was resected and drainage established. Died May 7, 1918. Autopsy May 7, 1918, 5 hours after death.

Anatomical Diagnosis: Interstitial bronchopneumonia (right). Empyema with operative drainage and multiple encapsulated residual collections of pus. Fresh fibrinopurulent pleurisy (left).

Left pleural cavity.—Contains about 1,500 cc. of opalescent yellow fluid, with shreds of fibrin. The surface is covered with a very thick layer of loose shaggy

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fibrin which stretches across the cavity in great ropes. The lung is slightly adherent at the apex and that portion is fairly voluminous. The rest of the lung is plastered against the mesial surface of the cavity and is entirely collapsed. The lower lobe is adherent to the diaphragm and to the posterior wall of the pleura by fresh fibrinous adhesions. *Right pleural cavity.*—The upper lobe of the lung is adherent by frail adhesions obliterating that part of the pleural cavity. There are dense adhesions over the lower posterior border of this lobe and the posterior part of the lower. There is a pocket of greenish yellow pus between the pericardium and the mesial border of the middle lobe. Over the 2nd and 3rd ribs there is a distinct pocket of pus which on removal of the lung is left between two layers of the parietal pleura. Small pockets exist between the base of the lung and the diaphragm. *Left lung.*—The lung is practically completely collapsed except at the apices of the lobes and is covered with a thick fibrinous exudate. Inflation with air does not completely distend the whole lung, leaving patches of collapse in the lower and posterior parts of both lobes. There are some indefinite projecting greyish nodules in the posterior part of the lower lobe, but otherwise there is no consolidation. *Right lung.*—The lung is heavy. The anterior portions of all lobes appear to be air-containing. The bronchial glands are large, dark greyish red, and pigmented. The surface of the lung is torn by separation of old adhesions and cannot be inflated. On section the upper lobe is normal in texture and air-containing. The lower lobe is also air-containing except in the lower part which is pasty and airless and presents some pale yellowish grey projecting nodules. The bronchi are not conspicuously thickened in the rest of the lung.

Cultures at autopsy showed *Streptococcus hæmolyticus* in the heart's blood and right and left pleura. Those from the lungs were sterile.

Microscopic Examination.—The left lung is fairly well distended. The pleura is thickened and freshly vascularized and has lost its covering layer of cells. The fibrin has been rubbed off in the section. The tissue itself shows no conspicuous interlobular septa, but all the bronchioles contain purulent exudate and show infiltration of their walls which is sometimes quite marked. The alveoli contain some fluid and some desquamated cells, but except in the neighborhood of the bronchioles they are little altered.

The right lung is covered with a thick layer of granulation tissue with fibrin. The interlobular septa are much more prominent than those of the left. The bronchi in a section from the lower border of the lower lobe are all much infiltrated with mononuclears and filled with purulent exudate. The alveolar walls are greatly thickened everywhere and infiltrated with mononuclear cells, but they are all collapsed and contain no exudate except a few desquamated epithelial cells. The lymphatics are in places filled with leucocytes, but are not prominent. This appears to explain the gross appearance of such a lung which is soft and flabby and rather satiny upon the cut surface. It is easy to recognize the fact that it is collapsed and not filled with a fibrinous exudate, but the thickening of the alveolar walls is likely to escape the unaided eye.

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Case 178.—C. A., age 28 yrs. Began Apr. 22, 1918, with typical measles, coryza, conjunctivitis, and red macular rash over body and face. On May 5, began to have cough with sputum, and some dyspnea with cyanosis. There was no definite dulness over the lungs, but râles could be heard everywhere. Voice became husky and at times was only a harsh whisper. By a great effort he could produce a tone. Sputum yellow, mucopurulent; loaded with Gram-positive cocci which grew with slight hemolysis, thought to be staphylococcus. Influenza bacillus also present. Blood cultures on May 7 and 9 negative. Died May 9, 1918, 4 days after the onset of the cough. Autopsy 13 hours after death, May 10, 1918, 9 a.m.

Anatomical Diagnosis: Clinical history of measles. Interstitial bronchopneumonia (bilateral). Lobular pneumonia. Ulcerative laryngitis.

Left pleural cavity.—Contains no excess of fluid; surfaces are smooth and glistening. *Right pleural cavity.*—Contains no excess of fluid. Surfaces are bright and glistening throughout. There are no adhesions. The lungs are voluminous and do not collapse. *Left lung.*—Readily inflated in all parts. On section it is air-containing everywhere except for a few small areas in the upper lobe which stand up above the surrounding lung tissue as greyish red elevated patches. In these the alveoli appear to be filled with exudate. Throughout the remainder there are small grey nodules which project slightly and are surrounded by hemorrhage. These prove to be bronchi with purulent contents, thickened grey wall, and hemorrhagic halo. They become more numerous in the lower lobe and are especially striking in the posterior part of the lung. *Right lung (Fig. 21).*—There are firm nodules to be felt all through the lung. Some appear on section as greyish red elevated patches with surface roughened by alveolar plugs. In the upper lobe there are a few greyish nodules with central depression surrounded by a broad hemorrhagic zone. These nodules which are much more numerous in the lower lobe are traceable to the termination of the bronchi which upon being opened are found to be filled with a purulent fluid. In the anterior portion of the upper lobe and through the middle lobe these nodules are visible but appear to be in an even fresher state and are represented by small bronchioles with slightly thickened walls and no hemorrhages. *Organs of the neck.*—The whole pharynx, including the base of the tongue, the tonsils, the posterior wall, and the pyriform sinuses, is intensely reddened. The epiglottis is also bright red, but on its posterior surface this color is mottled with small yellowish opaque areas with fairly smooth surface. There are deep ulcerations of the vocal cords on each side (Fig. 22), extending into the sinuses and on to the false vocal cords.

Cultures at autopsy gave *Streptococcus hæmolyticus* from the heart's blood and right lung. Streptococci were abundant in the film from the ulcer of the vocal cords. Cultures from the spleen were sterile.

Microscopic Examination.—The lungs are about alike. The pleura is only slightly altered in that it is hyperemic and sparsely infiltrated with mononuclear cells. There is nothing left of the covering layer of cells, but no fibrin can be seen

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on the surface. The interlobular septa are very wide and large lymphatics can be traced from the pleura into them. One or two of these show plainly by the direction of their valves away from the pleura at a point about 2 mm. from the pleural surface (Fig. 23) that the direction of the lymph stream is from the pleura towards the hilum. They contain only fluid, but streptococci are to be found in them in short chains and pairs. In places streptococci in numbers can be traced into the substance of the pleura. The interlobular septa as they pass deeper into the lung are edematous and contain a dense network of fibrin in which are entangled many mononuclear cells. Two types of lesions are found in the lung, one representing the acute lobular pneumonia, the other an early stage of interstitial bronchopneumonia. There are only a few patches of the former, while the latter is almost universal throughout the lung. Where the lobular pneumonia occurs the changes in the bronchioles tend to be the same as elsewhere, but are rather masked by the diffuse pneumonia.

These patches are fairly sharply outlined by small interlobular septa. They show a uniform filling of the alveoli with an exudate composed of blood, fibrin, and nucleated cells. Most of these cells are polymorphonuclear leucocytes, but some are desquamated epithelial cells, while many are similar to lymphocytes or are rather larger. The alveolar walls are not thickened as a rule, but in the neighborhood of the interlobular septa they, like these septa, are infiltrated with similar mononuclears. Streptococci are present in great numbers and appear in chains entangled in the fibrin, loose among the cells, or sometimes enclosed in cells. They are especially numerous in the alveoli which border on the septa. Where they lie amid red corpuscles, these have lost their hemoglobin and contrast sharply with those in the adjacent blood vessels.

In other parts of the lungs the lesions (Fig. 24) are concentrated about the small bronchi leaving considerable intervening patches of air-containing tissue with thin walled alveoli; the bronchioles are packed with a mass of cells and streptococci. The bacteria are ranged along the walls in clumps and strands. The cells in this exudate are much fragmented and distorted and it is difficult to determine their nature, but it is certain that while many of them are polymorphonuclear leucocytes nearly as many are mononuclear wandering cells. They are held in a network of fibrin. The epithelium of the bronchi is lost and they are lined by a thin layer of coagulated necrotic material. The wall is edematous and spread out and densely infiltrated with mononuclear cells. The blood vessels are distended, but the process is fresh and the wall does not look like granulation tissue with radially arranged blood vessels, as is the case in some instances in which the disease has been of long duration. The lymphatics in the outer part of the bronchial wall are wide and closely packed with leucocytes, mononuclear cells, and bacteria. The adjacent and continuous alveoli have walls which are slightly thickened by mononuclear infiltration. They are filled with dense fibrin containing distorted cells, some of which are polymorphonuclear, while many can be recognized as mononuclear cells. Red blood cells are frequent in these,

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and in the more distant alveoli are present in great quantities. Practically no bacteria are found in the exudate in these alveoli. The blood vessels are not especially changed. The bronchial glands are large, the lymph cords very wide and evidently containing many new cells. But the sinuses are especially widened and packed with mononuclear cells and leucocytes. They contain great quantities of streptococci often scattered diffusely but quite often in dense clumps. Streptococci are strewn along the surface of the mucosa of the trachea and are undoubtedly present in enormous numbers in the ulcerations of the vocal cords and other parts of the larynx. This specimen has not been cut for microscopic study.

Case 184.—J. B., age 22 yrs. Negro. On Apr. 29, 1918, had measles. On May 2 he was found to present the physical signs of lobar pneumonia with consolidation of the left lower lobe, dulness, bronchial breathing with a few large râles. Sputum bloody. Sputum on May 8 was mucopurulent and nummular, containing Gram-positive cocci. Cultures showed *Streptococcus hæmolyticus* and *Staphylococcus aureus*. Blood culture was negative on May 7. Temperature high at the beginning, 104–105°, later reduced to 101°. Leucocytes 9,000. Died May 10, 1918, at 9.45 p.m. Autopsy 38 hours after death. The body had been embalmed so that cultures failed to grow.

Anatomical Diagnosis: Interstitial bronchopneumonia (bilateral) with disseminated lobular pneumonia. Ulcerative laryngitis.

Left pleural cavity.—Contains about 10 cc. of fluid. The surfaces are clear and smooth. *Right pleural cavity.*—Contains no fluid. The surfaces are smooth. *Left lung.*—The lung is blue and heavy in the posterior portion, but both lobes are air-containing anteriorly. Upon artificial insufflation both lobes are pretty well distended but firm nodules can be felt which on section project above the cut surface (Fig. 25). They are grey, rough, and granular, and when cut in certain directions show a central lumen. In the lower part of the lung they are almost confluent and are embedded in deeply hemorrhagic collapsed patches. The bronchi are deeply reddened and dilated in their peripheral parts where they are filled with a bloody purulent exudate. The nodular consolidations which lie about their terminal portions are much more numerous and more nearly confluent in the posterior part of the lung. The bronchial glands are enlarged, greyish red, and firm. *Right lung.*—The lung is smooth superficially, but there are a few hemorrhages in the pleura between the lobes. The lower lobe is heavy and nodules can be felt throughout it. The middle lobe is collapsed posteriorly but inflated anteriorly. The upper lobe is more air-containing but also feels nodular. In the upper lobe on section it is found that the bronchi are thickened, reddened, and dilated at their ends. They are accompanied or surrounded by elevated consolidated areas which are ragged in outline and rough and spongy. The bronchial walls are opaque and lined with a dull grey material. The finer bronchioles still appear as lumina in the centers of consolidated areas which are surrounded by hemorrhagic zones. Such lesions are found in the posterior part of the middle lobe and

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more abundantly in the lower lobe where they tend to become confluent. *Pharynx and larynx* (*Fig. 26*).—The tonsils are not especially enlarged. The pharyngeal wall is reddened and the left side of the epiglottis and left arytenoepiglottic fold and adjacent tissues are edematous. There is definite ulceration of the vocal cords and there are other ulcerations below them which extend on the walls of the larynx. There are quite deep ulcerations at the base of the epiglottis. The tracheal mucosa is much reddened.

Microscopic Examination.—The lung shows a combination of the lesions of interstitial bronchopneumonia and lobular pneumonia. The pleura is not thickened and shows no evidence of fibrin on its surfaces. The interlobular septa are quite inconspicuous and none of them shows any special edema or infiltration, or even the distension of the lymphatics.

The bronchi on the contrary are wide and very conspicuous (Fig. 27). Each branch is surrounded by a denser lung tissue, but there are some other patches of consolidation which extend away from the bronchi. There is a ragged mass of debris in the lumen of each. This contains many red corpuscles, polymorphonuclear leucocytes, as well as fragments of necrotic cells. Streptococci in tangled masses are ranged along the walls of the bronchi, but there are no influenza bacilli. The epithelium is entirely destroyed and in its place there is a rather thick layer of coagulated necrotic tissue. Outside this in the larger bronchial branches there are remains of mucus glands, etc. In general the wall has assumed the character of a loose edematous granulation tissue with abundant wide blood vessels arranged more or less radially and a profuse infiltration with mononuclear wandering cells of various sizes. If this granulation tissue is in any way derived from the swelling and spreading apart of the lymphoid tissue in the wall of the bronchus, which has occurred to me as a possibility, it must at least have undergone an extraordinary change. Lymphoid tissue can be seen at certain points, but it does not form in this case as in some others a complete mantle about the bronchi, and most of the bronchial wall seems actually to be composed of granulation tissue. The lymphatics in the outer layer of the wall are wide and generally filled with a clot which entangles red corpuscles, mononuclear cells, and chains of streptococci. The adjacent lung tissue is consolidated by the filling of the alveoli with dense fibrin in which there are to be found a few desquamated epithelial cells and mononuclear wandering cells. It is striking that the epithelial cells when not desquamated are much more nearly cubical than normal, and among these plump cells one may find mitotic figures (Fig. 28). The alveolar walls are thickened also and are infiltrated with mononuclear cells. This is not extreme, however, and a much more remarkable infiltration of this sort is found in the walls of small vessels in such a neighborhood.

The other areas of consolidation mentioned above as not so intimately related to the bronchial thickening are patches in which the interstitial changes are slightly developed but in which all the alveoli are filled with dense masses of polymorphonuclear leucocytes in a delicate network of fibrin or alone (Fig. 29).

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Among these there are enormous numbers of streptococci, although there are none in the denser plugs found in the alveoli about the bronchi. These areas fade at the margin into patches of edema. There are quite extensive areas in which the thin walled alveoli are distended with fluid without any cells and in these alveoli too, chains of streptococci are found.

Case 191.—S. F., age 22 yrs. Negro. No history of previous illness. No record of measles. Began suddenly on Apr. 13, 1918, with pain in chest and chill. Diagnosis of lobar pneumonia involving left lower lobe was made, and later, on May 5, there was found also a lobar consolidation of the right lower lobe. The existence of empyema on the right side was recognized by aspiration on May 13. A yellow serum with greenish white sediment loaded with streptococci in short chains was removed. These proved to be *Streptococcus hæmolyticus*. Blood cultures on May 11 were negative. Died May 14 at 5.30 p.m. Autopsy May 15, 1918.

Anatomical Diagnosis: Interstitial bronchopneumonia (left lower and right upper and lower lobes). Disseminated lobular pneumonia. Empyema (right).

Left pleural cavity.—Contains no excess of fluid. There are a few fresh adhesions over the lower edge of the upper lobe. The surface of the pleura is dull. *Right pleural cavity.*—Contains about 700 cc. of thick greenish yellow pus which is distributed in the space between the lung and the pericardial sac, in the meshes of adhesions between the lung and diaphragm, and about the apex of the lung. There are easily torn adhesions over the back of the lung which seem to separate into spaces which are filled with purulent fluid. *Pericardium.*—Contains no excess of fluid and the lining surfaces are smooth, but there are bright petechial hemorrhages over the posterior surface of the heart with shreds of fibrinous material overlying them. *Left lung (Fig. 30).*—The posterior surface is roughened by fibrin especially over the lower lobe and between the lobes. The upper and anterior part of the upper lobe is air-containing, but the posterior and lower part is firmer. On section, although this lobe is easily inflated, there are found in the lower portion numerous firm projecting nodules surrounded by hemorrhagic zones. The lower lobe contains only a little air-holding lung tissue and is not inflated by attempts to blow air into it. On section it is found to be thickly studded almost everywhere, but especially in the lower part, with nodules which are surrounded by hemorrhage and show a central depression which corresponds with the lumen of the bronchiole. The bronchial glands are enlarged and greyish red. *Right lung.*—The surface and the interlobar spaces are occupied by fibrin as described. The whole lung is collapsed and flabby except for a small portion of the anterior half of the upper lobe. Even after inflation the lower portion of this lobe is collapsed and shows numerous bronchi with thickened walls which appear as definite nodules. In the lower lobe collapse is extensive and there are many greyish nodules which surround the lumina of bronchi. There is also some patchy consolidation of a deep greyish red color rather different in appearance from the nodules. *Pharynx and larynx.*—There is slight reddening throughout, but no

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ulceration of the vocal cords although there is a discoloration as though from a healed ulceration just below the cords.

Cultures at autopsy gave *Streptococcus hæmolyticus* in pure culture in the heart's blood, right and left lung, right pleura, and pericardium.

Microscopic Examination.—The right lung shows a thick pleura composed of highly vascularized granulation tissue covered with fibrin. There are streptococci on the surface of the fibrin. The interlobular septa are not much widened but the lymphatics are slightly distended with clots which contain leucocytes and fibrin.

The bronchi are full of half necrotic leucocytes with abundant streptococci and influenza bacilli. The epithelium is largely desquamated and the walls are converted into a vascular granulation tissue which is much infiltrated with mononuclear cells, evidently derived in part from a thickening of the lymphoid tissue of the wall.

The alveolar walls are not thickened or infiltrated. The alveoli are mostly collapsed, their walls very hyperemic. Those near the bronchi are free of blood and their walls are sometimes infiltrated with red corpuscles. Many of the nearby alveoli are partly filled with desquamated epithelial cells, but there is also a great deal of fluid. Some contain dense plugs of fibrin which have undergone little or no organization. Hemorrhage is widespread about these bronchioles.

In many places the bronchi are surrounded by patches of lung tissue in which the alveoli are filled with leucocytes whose polymorphous nucleus is plain. These are often studded with streptococci. Indeed in some places the alveolar walls have become necrotic. Some of these areas of lobular pneumonia are extensive and no doubt necrosis of the tissue occurs commonly in the larger ones.

Case 193.—A. M. M., age 23 yrs. Began suddenly without previous illness or history of measles on May 3, 1918, with chill and fever. On May 5 the diagnosis of lobar pneumonia was made with involvement of the left upper lobe. Sputum on May 8 was tenacious and mucoid without blood, and contained Gram-positive diplococci which proved to be Pneumococcus Type III. *Staphylococcus aureus* was also present. Blood culture on May 8 showed a few non-hemolytic streptococci. Another on May 9 was negative. Died May 16, 1918, at 8.15 a.m. Autopsy May 17, 1918, 21 hours after death.

Anatomical Diagnosis: Old interstitial bronchopneumonia with abscess formation (left upper lobe). Fibrinous pleuritis. Hyaline degeneration of rectus abdominis muscle.

Left pleural cavity.—Contains no fluid. The surfaces are smooth except that the posterior part of the upper lobe is adherent to the costal pleura by easily broken adhesions, and the base of the lung to the diaphragm by old adhesions. *Right pleural cavity.*—The cavity is almost entirely obliterated by old adhesions which are especially dense between lung and pericardial sac, and between the base of the lung and the diaphragm. *Left lung.*—The lung is voluminous and in the upper lobe there can be felt a solid mass occupying the upper

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posterior part. The pleura has lost its gloss over the solid part but is smooth over the anterior part which is air-containing. On section the consolidation is fairly uniform, pale greyish red, and presents a rather rough surface which is distinctly translucent. The lower part is perhaps slightly redder than the upper. About the middle of this lobe there is a large abscess cavity reaching practically to the pleura but not perforating it. This cavity measures 5 cm. in diameter, is of extremely irregular outline with lateral excavations, and communicates widely with the large bronchus which opens abruptly into it. It contains a yellowish purulent exudate and there is a shreddy dark greenish grey necrotic tissue hanging from the wall. The wall is made up of a thin line of opaque yellowish material. In the anterior part of the upper lobe the interlobular septa are quite distinct. In places there are small grey projecting nodules related to the bronchi. The lower lobe is air-containing throughout. The bronchial glands are large, pale, and greyish, and studded with pigment. The large bronchi contain a thick frothy mucopurulent exudate. *Right lung.*—The lung is torn in removal and roughened by old adhesions, but it is air-containing throughout and of normal texture. The bronchial glands are not enlarged. *Pharynx and larynx.*—Normal.

Cultures taken at autopsy showed *Streptococcus hæmolyticus* in the heart's blood and left lung.

Microscopic Examination.—The tissues of the upper lobe of the left lung show most advanced changes. The pleura is thickened and dense and is covered with a thin layer of fibrin. The interlobular septa and the whole connective tissue framework of the lung are enormously thickened and condensed. There has evidently been a great new formation of connective tissue, for this widening is not due to edema but to the formation of closely knit fibrous tissue. The lymphatics are wide and in places contain some free cells, but most of them are partly or completely obstructed by masses of vascularized connective tissue which have evidently resulted from the organization of thrombi formed in the lymphatics at an earlier stage. The bronchi are filled with purulent exudate which contains large numbers of streptococci. The epithelium is in general preserved, but the walls are greatly thickened both by new formation of connective tissue and a dense infiltration of mononuclear cells. Lymphatics in their walls are in places obliterated by newly formed connective tissue. The alveolar walls are thickened everywhere, partly by infiltration of wandering cells but partly by newly formed connective tissue. They are in most places filled with a mass of desquamated epithelium, some mononuclear cells and leucocytes, and fluid. Fibrin is not so conspicuous as usual, but perhaps chiefly because most of it is replaced by strands of connective tissue which fill the alveoli in places. The epithelium when it is preserved is high and cubical. Red blood corpuscles are abundant in places so that the alveoli are full of blood. The most striking feature, therefore, is the advanced interstitial infiltration and induration together with the organization of the exudate both in the alveoli and lymphatics. One section passes

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through the abscess which is filled with polymorphonuclear leucocytes with bacteria. The lining layer of the cavity is densely infiltrated with large vacuolated cells. Outside this layer the lung tissue for some distance is much indurated and every alveolus is filled with a solid plug of connective tissue. Organization has evidently proceeded rapidly here. Sections through other parts of the lung show it to be air-containing, but the septa and perivascular and peribronchial tissues are greatly thickened and some alveoli are filled with desquamated cells and wandering cells. Lymphatics in the septa in this part of the lung (lower left lobe) contain abundant leucocytes and fibrin.

The rectus abdominis muscle which appeared normal to the unaided eye shows most extensive hyaline degeneration and disintegration of the muscle fibers which are broken into formless clumps. These are surrounded by nuclei many of which are undoubtedly the nuclei of the sarcolemma. These sometimes appear to coalesce into giant cells. But there is also a definite reaction on the part of the interstitial tissue and blood vessels and numerous mononuclear phagocytes are present.

In attempting to present these diseased conditions according to their etiological agents, if we group the cases of pneumonia which are caused by the hemolytic streptococcus in several classes so as to emphasize one or the other of the predominant lesions, it is only to facilitate the description of that lesion, as one might describe separately tuberculous pneumonia and miliary tuberculosis of the lung. The combination of the streptococcal lesions is almost as common as the occurrence of several types of tuberculous lesion in the same lung. In the group of cases just described the attempt has been made to select those which show in its purest form the so called interstitial bronchopneumonia, but even so some trace of lobular pneumonia can be found in all but a few. Nevertheless, in whatever combination they occur, even when associated in the same lung with the lobar pneumonia caused by the pneumococcus the characteristics of the interstitial bronchopneumonia stand out distinctly.

The typical change in the pleura consists in the effusion of a large quantity of thin turbid fluid into the pleural cavity. This is usually brownish with a fine granular sediment which is stirred up on moving the lung, but there are generally also floating shreds of fibrin. The surface of the pleural membranes is covered with fibrin under which hemorrhages are often visible. It is remarkable, however, that thickening of the pleura by the formation of new granulation tissue

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takes place very rapidly. This is a common condition, but there are cases, especially those in which adhesions had existed, in which there is no exudation, and others of recent origin in which although the lungs are diffusely affected the pleural surfaces are perfectly smooth and the cavity is practically dry. There are various later modifications of the character and distribution of the effusion leading to its encapsulation and to a more definitely purulent character which forms the rule in cases which survive long enough. In view of the interest devoted by surgeons to the question of empyema, an analysis of the condition in all the cases in this series will be given later in this paper.

The gross appearance of the lungs in the cases of interstitial bronchopneumonia varies with the age of the lesion. The powers of resistance of the individual doubtless have much to do with this also, and it seems that in those with little resistance the type of lesion is different and tends to the lobular form. At first it seemed merely a surmise that the lesions confined to the bronchioles and their immediate environment were early changes, since some cases, such as No. 14, showed these very slight alterations in one lung in a patient in whom the other lung was in an advanced stage. Nevertheless, the occurrence of death after 7, 4, 8, and 7 days of pulmonary involvement in Cases 32, 178, 184, and 194 has shown that what appeared to be fresh lesions really do occur in the cases of briefest course. The early lesions in the opposite lung in older cases must simply represent fresh lesions in a case in which elsewhere similar changes have long been developed.

The lung may be collapsed, since that is largely an effect of the pressure of a large pleural effusion, or, as in Case 32, both lungs may be distended with air.[2] In such a case as No. 32 the lesions appear as minute projecting nodules often grouped in twos and threes, several being found within the area of a lobule. In Cases 14 and 194 these small lesions show the branching of the terminal bronchioles and are

[2] When the lung is inflated artificially with air it is easy to see the lesions which are submerged in the general blue-grey of the collapsed area. For that reason we have frequently blown up these lungs with a bulb tied into the bronchus spreading open the collapsed alveoli and aerating the blood in their capillaries so that it becomes bright red. Then the actual lesions become very distinct.

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rendered conspicuous by their halo of hemorrhage. In Case 178 this became very brilliant since each bronchus could be traced often in complete longitudinal section by the grey thick wall, its yellow contents, and its envelope of hemorrhage.

In Case 37, which was of 16 days duration, there was no extensive peribronchial consolidation, but the bronchi were so greatly thickened as to project in firm tubercle-like nodules.

In Cases 29 and 34, of 20 and 14 days duration, the lesions expand from the bronchi into patches of firm yellowish consolidation 3 to 5 mm. in diameter which project as nodules on the cut surface. The intervening lung substance in such cases, aside from the hemorrhage spread around these peribronchial nodules, is greyish, elastic, and edematous, while the interlobular septa are thickened, yellow or white, and opaque, and stand up like low stone walls which separate fields. They divide the cut surface into startlingly distinct lobules and in each of these there are several nodules. In Case 41 there are the most advanced lesions, although the course of the disease was only 17 days. Not only are the bronchi enormously thickened, but the peribronchial nodules of consolidation are larger than in any other case and stand out as firm dense and perfectly homogeneous yellow elevated patches, each with its central bronchiole and its halo of hemorrhage. In one or two of the cases of long duration, Nos. 167 and 181, which lasted 23 and 46 days, and in one of the fresher cases, No. 193, which lasted only 14 days, we found abscesses with actual cavity formation, the contents of the necrotic areas being discharged through the bronchi. This is a frequent occurrence in the cases of lobular pneumonia and remains to be described in other cases, but it is not so frequent in those in which the lesion takes the form of the interstitial bronchopneumonia. The essential features, therefore, in the gross appearance of the lungs in interstitial bronchopneumonia lie in the filling of the bronchioles with opaque exudate, the thickening of their walls, and the consolidation of the adjacent lung tissue which appears in cross-section as a nodule, in longitudinal section as a branching mantle of dense tissue bordered with hemorrhage accompanying the bronchiole. Atelectasis of the intervening lung substance, great thickening and prominence of the interlobular septa and pleura, and usually pleurisy with abundant effusion make up the whole picture.

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The bronchial glands are somewhat enlarged and soft. The mucosa of the large bronchi is deeply reddened and covered with purulent exudate, sometimes with a necrotic pseudomembrane. Some writers have insisted that this should be called purulent bronchitis or bronchiolitis, but the involvement of the whole lung takes place so promptly, including the framework and the pleura, that I think the term bronchopneumonia is better justified.

The microscopic study of the early changes shows essentially an infection of the bronchi with streptococci. The greatest stress should be laid upon the staining of bacteria in the tissues because it is only in that way and not by mere report of the presence of cultivable streptococci that we may determine the exact topographical relation of these organisms or others to the lesion.[3] It is found that in every

[3] A new stain which is a combination of Goodpasture's and the Weigert fibrin stain has served well to demonstrate in the tissues Gram-negative organisms, such as the influenza bacillus, in red and Gram-positive bacteria in blue. During the correction of the proof of this paper the cases have been restudied with this stain. It is as follows:

1. Stain for 10 minutes to ½ hour or more in Goodpasture's stain, which is:

	cc.
30 per cent alcohol	100.0
Basic fuchsin	0.59
Aniline oil	1.0
Phenol crystals	1.0

2. Wash in water.
3. Differentiate in 40 per cent formaldehyde solution (pure formalin). This requires only a few seconds. The bright red color washes away and gives place to a clear rose color.
4. Wash in water.
5. Counterstain in saturated aqueous picric acid. The section should remain until it assumes a purplish yellow color, about 3 to 5 minutes or less.
6. Wash in water.
7. Differentiate in 95 per cent alcohol. The red color reappears and some of it is washed out. Some of the yellow of the picric acid is also washed out.
8. Wash in water.
9. Stain in Stirling's gentian violet 5 minutes or more.
10. Wash in water.
11. Gram's iodine solution.
12. Blot dry without washing.
13. Aniline oil and xylol (equal parts) until no more color comes away.

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instance the streptococci are present in numbers among the leucocytes which fill the bronchioles. They can be traced along the mucosa of the larger bronchi up into the trachea where possibly other bacteria may also be found, but in the terminal bronchioles there are in many instances only streptococci. In some cases there are relatively few, while in others, such as Nos. 184 and 178, they are present in tangled masses strewn along the mucosa but in smaller numbers in the center of the bronchial lumen. Recent papers from England and France, already referred to, declare for the preponderant part played by the influenza bacillus. A glance at the table given above will show that it has been found quite commonly in the sputum in these cases too, sometimes in the lung and pleural fluid. Its relation to these lesions must be left in some doubt since it is present in only part of the cases while the streptococcus is invariably present. The British writers describe a purulent bronchitis or bronchopneumonia which resembles this most closely and regard it as due to the influenza bacillus, although they frequently found an associated *Streptococcus pneumoniæ* (pneumococcus) and *Streptococcus longus*.[4]

The epithelium of the bronchus is usually intact, but in some cases, Nos. 178 and 184, it is quite destroyed and even the underlying tissue is necrotic for a considerable depth. This appears to the naked eye as an opaque greyish yellow pseudomembrane lining the bronchus down to the finest ramification and extending out to the largest branches. In the earliest stages, as in Case 32, the respiratory bronchioles are the ones affected, while the larger bronchi show little

14. Two changes of xylol.
15. Balsam.

Gram-negative organisms are red, Gram-positive blue.

Dr. Goodpasture's own method is not yet published but he kindly allows me to use his formula in describing this method. Goodpasture's stain corresponds with the first seven maneuvers given above.

[4] During the epidemic of influenza which raged through September and October, 1918, we have encountered cases in which the influenza bacillus occurred in pure culture in the lungs and bronchi. In these the lesions resembled very closely those which are described here under the name interstitial bronchopneumonia. (Note made during the correction of the proof.)

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change. Leucocytes with streptococci extend out into the lateral vestibules and into the terminal ones and even into the ultimate alveoli. There is little other change, but although the more distant alveoli are not altered, the bronchial wall and the adjacent alveolar walls even at this stage are infiltrated with wandering cells. There are few of them at this stage, but they give a distinct character which comes out clearly in later stages.

In all the later stages this change in the connective tissue, elastic tissue, and musculature which make up the wall of the bronchus is striking. The normal elements are spread apart by great numbers of mononuclear cells which intercalate themselves between the fibers and often form a mass which lifts up and dislodges the epithelium. Most of these cells are small like lymphoid cells, but many are larger, occasionally assuming the character of plasma cells or the various types of larger mononuclear wandering cells. Edema accompanies them and aids in the spreading apart of the connective tissue. The blood vessels are distended with blood and evidently new ones are formed with associated fibroblasts, for in many cases the wall assumes the appearance of a highly vascular granulation tissue in which the blood vessels come to be radially placed. In some cases the bronchi become dilated, occasionally to a marked degree, as in Case 181, and to a less extent in Cases 41 and 184. In the most advanced conditions, as in Case 41, the walls of the bronchioles become enormously thickened and form a compact tube of infiltrated tissue, but in most instances the wall is rather relaxed and loose in texture. With dilatation the epithelium may be stretched and flattened or it may disappear by being desquamated, leaving the surface of the new granulation tissue exposed.

The normal wall of the smaller bronchi contains only a relatively small amount of lymphoid tissue, scattered in thin strands in its outer layers, except at certain places such as the points of division where somewhat more compact masses often occur. About the same may be said of the adventitia of the blood vessels and the interlobular septa. It seems possible, however, that much of the infiltration which has been described, and a part of the thickening of the bronchial wall may be due to the swelling and spread of the lymphoid tissue all along the wall of the bronchus, and its appearance of being a new growth of

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granulation tissue with radially arranged and abundant blood vessels may well be explained in the same way, since with a greatly thickened mantle of lymphoid tissue there would arise a more conspicuous vascular supply for that tissue.

The lymphatics which run in the bronchial wall are distended with leucocytes, mononuclear cells, and blood, and usually thrombosed with great quantities of streptococci entangled in the thrombus. Before discussing other parts of the lymphatic network, however, we must describe the alveolar structure of the lung.

It has been said that in the earliest stages the alveoli about the terminal bronchioles contain leucocytes and streptococci. That seems to be a transient condition, however, for in stages only a little older a different condition is found. Even in the early lesions in Case 14, in which the opposite lung showed old lesions, the bronchiole is distinctly infiltrated and thickened, and the affection extends through the wall to the adjacent alveoli. These are filled with blood, the lining epithelium is beginning to desquamate, and there are some mononuclear cells.

In the later stages a uniform process appears which is a combination of these. The alveolar walls contiguous to the bronchi become widened and thickened by an invasion of mononuclear cells just as in the bronchial wall itself. The alveoli are partly filled with fluid and with desquamated alveolar epithelium. Many of them a little farther removed are quite filled with red corpuscles and all contain dense masses of compact fibrin in which cells are partly entangled. Mononuclear cells escape into the alveoli, but in small numbers. It is strange that although streptococci are found in the lumen of the bronchus among the polymorphonuclear cells which persist there, and in still greater numbers in the thrombosed lymphatics of the wall, they are not to be found in these distended alveoli, which seems to show that this process has a certain protective influence.

A later stage, as in Cases 29, 15, 16, 34, or best of all 41, shows the wide extension of this process of filling up the alveoli with dense fibrin in solid but rather contracted plugs which occupy only part of the space, epithelial cells, fluid, and blood. The fluid which extends far wide of the actual area of consolidation is evidently very thick and viscous, for it coagulates in fixation into a brittle mass

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which takes a deep stain. The infiltration of the alveolar walls sometimes produces a great thickening. The cells accumulate on each side of the centrally placed layer of capillaries and lift away from them the delicate structureless membrane which on each side forms the wall of the alveolus upon which the epithelial cells are laid. This is very distinct in spite of the text-book statement that there is but one structureless membrane in each alveolar wall. This infiltration is most marked in the immediate neighborhood of the bronchiole, in the neighborhood of blood vessels whose adventitial walls are thickened in the same way, and again in the neighborhood of the pleura and the interlobular septa. In other parts of the lobule the alveolar walls maintain their proper thickness for a long time and in many cases are air-containing and normal in appearance where they lie apart from the foci of consolidation. Where the alveolar walls are rendered dense and not easily stretched, the alveolar epithelium becomes thick and cubical; frequently one may find mitotic figures in these cells, indicating plainly their active multiplication which must be necessary to produce such numbers as are found shed into the cavities of the alveoli. It is astounding to find that even before the later stages just described have been reached, organization of the exudate has begun. In the bronchioles of the tiny hemorrhagic foci in Case 14, and in the alveoli and bronchi of many of the other cases, new blood vessels are found to have grown into the exudate carrying fibroblasts and replacing the fibrin with vascular connective tissue. The origin of this from the walls of the bronchioles and its extension into many alveoli is often seen. Connective tissue may spring up through a defect in the epithelium of the bronchial wall and stretch across the lumen to connect with the opposite wall or it may form a column which reaches down into the alveoli and forms a sort of mold of the original air spaces. Epithelium grows over it rapidly and whole fields may show the alveoli fairly occupied by strands of pretty dense connective tissue, supplied with blood vessels and clothed in epithelium.

The blood vessels of the lung are not especially altered. I have found none thrombosed, and the circulation is unimpaired. The circulation is indirectly embarrassed in two ways by the same means. The obstruction of the bronchi by infected material need not extend

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into the alveoli of its own respiratory district, although the inflammatory process extends through the wall to the neighboring alveoli, but it does prevent the entrance of air. The atelectasis which results from this is rendered general and complete by the pressure exerted on the lung by an effusion of fluid into the pleura, and the lung as it appears when removed from the body is commonly a flabby pasty soft grey-blue mass which has been plastered against the vertebral column and compressed into an airless substance. The blue color at once indicates its filling with venous blood, for when it is distended it quickly becomes bright red. This must be due to the angular kinking of the venules which prevents the proper egress of the blood. This is supported by the fact that in old cases of empyema in which the condition has lasted a long time the alveoli are filled with epithelial cells loaded with iron pigment which are so characteristic of chronic passive congestion. One may conclude that there is a chronic passive congestion, caused by local pressure which indicates that the passage of blood is impeded and necessarily the whole circulation in some degree obstructed.

The pleural changes have been mentioned. The pleura itself is sometimes smooth, sometimes covered with a thin film of fibrin, but most often with a thick shaggy layer of fibrin into which it throws up blood vessels and connective tissue, by this process converting itself into a thick layer of granulation tissue. This is, of course, continued into the pleural surfaces of the interlobar spaces where, however, it is limited by the ready formation of adhesions.

The interlobular septa which run downward into the lung from the pleura have become especially interesting in this disease because of their own changes and because of the lymphatics which run in their substance. The septa themselves become edematous and their connective tissue fibers are spread wide apart. A coagulum of fibrin in which there are entangled numerous mononuclear wandering cells forms in the fluid in the meshes of this tissue. At a later stage this condition which renders the septa very conspicuous, as in Cases 34 and 29 and others, gives place through abundant formation of new connective tissue to one in which the widened septa are found to be composed of dense fibrous tissue, as in Cases 35, 193, 57, 58, and others.

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The lymphatics of the lung have been the object of much study (Miller, Cunningham, and others), but even yet there is not perfect unanimity of opinion about their arrangement and more especially about the course of the stream of lymph. According to Miller's description, they run in the septa and in the walls of the blood vessels and bronchi toward the hilum of the lung where they empty into the sinuses of the bronchial glands. On the pleural surface, or rather in the substance of the pleural membrane, lymphatic channels which form a dense network are connected with those in the substance of the lungs. Miller states that the current from the superficial layers of the lung is directed away from the hilum and toward the pleural network and that this is supported by the direction of the valves toward that network. I have made some injections in distended lungs after having first filled the blood vessels with carmine gelatin. The lymphatics were injected with Berlin blue through a fine hypodermic needle inserted into the substance of the pleural membrane. A most extensive and complete injection of this network can be seen to shoot out over the surface of the lung and from it larger trunks dipping into the substance of the lung suddenly appear as they are filled with the blue mass. A fairly complete injection of the perivascular and peribronchial and septal lymphatics as far as the hilum of the lung can be made in this way, showing the latter channels to be very wide. It seems probable from experience with the injecting of lymphatics elsewhere that no such complete injection could be made with moderate pressure if many valves had to be forced backward. Further a fortunate section or two showing the lymphatics of the interlobular septa in direct connection with those of the pleural network reveals the fact that the undisturbed valvès actually open away from the pleura even at a distance of only a few millimeters from the surface. This is shown in Fig. 23. I think, therefore, that in the lymphatic apparatus of the lung the natural current is from the pleural surface toward the hilum of the lung.

In all the cases of interstitial bronchopneumonia, the lymphatics as seen in section, whether in the walls of the bronchi and blood vessels, in and about the interlobular septa, or in the pleura, become conspicuously dilated and are frequently filled with a thrombus. These thrombi are entirely analogous to thrombi which might form

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in veins except that they contain no red corpuscles and are not constructed on the peculiar framework of platelets which appear so regularly in the venous thrombi. Platelets, of course, must be practically absent from the fluid lymph in such peripheral lymphatics so that the materials for the construction of an elaborately formed thrombus are lacking. The lymphatic thrombi are mere formless coagula of fibrillated fibrin in which leucocytes and many streptococci are entangled. They must effectively obstruct the channel when they are large enough and thus divert the current into other paths.

In many cases the lymphatics distended in this way with opaque yellowish pus or clots loaded with leucocytes become most conspicuous on the cut surface of the lung. They are sometimes 2 to 3 mm. in width and distinctly beaded as they run along the course of the interlobular septum. Many of them can be traced to their connection with the pleural network which may be similarly distended with a yellowish white mass. On section, as shown in Fig. 10 from Case 34, they appear as huge varicosities in the course of the interlobular septum and are filled to distension with leucocytes and streptococci. In one lung which was shown me they were so large as to be mistaken for bronchi.

It seems that this constant infection of the peribronchial and other lymphatics in the early stages of the disease, with a real concentration of bacteria in the lymphatics, must play a part in the early production of pleural infection. Of course the idea of transportation of the bacteria by the lymph to the pleura is opposed by the statement made above that the current is all in the opposite direction, but with the entrance of the bacteria the lymphatics become obstructed and the current stops. Direct extension by growth is visible in these lymphatics in sections, and that seems to afford the most plausible explanation of the early infection of the pleura. Other arguments concerning pleurisy may be more satisfactorily discussed later in connection with empyema.

These then are the main points in the anatomy of the interstitial bronchopneumonia in as far as the lung is concerned. It appears as a primary infection of the bronchioles. In the course of the affection thickening and infiltration of the bronchial and alveolar walls, of the interlobular septa, perivascular adventitial tissue, and of the pleura

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occur. The lymphatics are widely infected and thrombosed. The alveoli about the infected bronchi are filled with fluid and blood, dense coagula of fibrin appear, the epithelial cells multiply and are shed into the lumen, a few mononuclear cells appear, and organization takes place in this exudate until bronchi and alveoli contain strands of fibrous tissue. In the meanwhile the infection probably extending by growth along the lymphatics reaches the pleura and sets up a pleurisy with effusion, one effect of which is to cause extensive collapse of the lung. It is important to consider at this point the distribution of the bacteria in the lung in this affection. The exudate in the lumen of each bronchiole always contains streptococci in considerable numbers; the lymphatics in the bronchial wall and those seen elsewhere contain them in numbers in the thrombi; the superficial layers of the exudate on the pleural surface contain a perfect feltwork of these organisms sometimes enclosed in leucocytes; but the contents of the alveoli and the substance of the tissue contain none. Even in the bronchial wall it is generally impossible to trace the bacteria into the crevices of the tissue. In the pleural exudate it is the superficial layers which contain them; the fluid exudate is a thick suspension of bacteria, but they are found in rapidly decreasing numbers as one passes into the substance of the fibrinous exudate, and in the pleural granulation tissue there are none. Since they find the conditions for their life so unsuitable in the depths of a fibrinous exudate there must be rapid additions to those in the lymphatics to maintain their numbers. It is interesting to observe their behavior upon the surface of the lobulated mediastinal fat which hangs in the pleural cavity near the apex of the heart. Wherever the surface was exposed the streptococci were numerous; where two folds had adhered so that the crevice between them was obliterated by a fibrinous adhesion the bacteria descended to the depth of the open crevice, but there were none in the deeper obliterated part, nor anywhere in that tissue.

All this must signify a definite power of resistance on the part of the tissues in these cases, indicating their ability to destroy the organisms whenever they come into sufficiently close contact with the living cells, for as we shall see in the next two groups of cases a different lesion is developed in those patients, apparently because they have little of this power of resistance. While streptococci are present in

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relatively small number in the interstitial form, in which bulwarks are built up against them, they swarm in direct contact with the tissues in the lobular pneumonia and cause extensive necrosis. The contrast between their distribution in interstitial bronchopneumonia and that of pneumococci in lobar pneumonia is also striking because the pneumococci are scattered evenly throughout the depths of a pleural exudate and everywhere in the contents of the alveoli.

Small foci of lobular pneumonia occur in many of these cases, but the next group is set apart as illustrating more fully this combination.

2. *Interstitial Bronchopneumonia and Lobular Pneumonia.*

Case 24.—A. G. C., age 25 yrs. Measles and mumps in childhood. Taken sick Jan. 15, 1918, with sudden pain in the right side. Next morning fever and extreme weakness. Entered hospital Jan. 16. Dulness over right lung in front with tubular breathing and râles. Left lung hyperresonant. Leucocytes 18,800. Temperature 98–105° F., pulse 94–155, respiration 20–55. Died Feb. 4. Autopsy Feb. 5, at 5 p.m.

Anatomical Diagnosis: Interstitial bronchopneumonia with disseminated lobular pneumonia.

Left pleural cavity.—Contains no fluid; surfaces are dull and hyperemic over the posterior portion of the lung. *Right pleural cavity.*—Contains no fluid. There are light fibrous adhesions easily broken through over the posterior portion, and the surfaces are injected. *Heart.*—The pericardial cavity contains a few cc. of fluid; its surfaces are glistening. The heart is of moderate size, flabby, and soft. The endocardium of the right side is smooth, tricuspid, and the pulmonary valves are delicate. The mitral valve is thickened and shortened but not definitely stenosed. The chordæ tendineæ are also involved in this thickening, but the mitral ring measures 8.5 cm. in circumference. On the anterior leaflet there are several massed vegetations which form a clump about 1 cm. in height. These are rough and crumbly. There is a smaller vegetation at the middle of the leaflet while the large mass extends somewhat on the posterior leaflet. The aortic valves are delicate and competent. The coronary arteries are smooth. In the myocardium of the septum beneath the endocardium is a small pale fleck surrounded by hemorrhage. *Left kidney.*—Contains an anemic infarction about 1 cm. in diameter. *Left lung.*—Voluminous. The upper lobe is easily and completely insufflated, the lower lobe less so, leaving superficial collapsed areas. On section the upper lobe is air-containing throughout. Lower lobe is spongy and apparently largely air-containing. There are coalescent grey spongy patches surrounding blood vessels or bronchi which are separated especially near the surface of the lung by deep red areas. There are no definite nodules nor

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even any definite consolidation. No distinct thickening of bronchial or blood vessel walls is to be observed and there is no pleurisy. *Right lung.*—Edematous and densely studded with greyish nodules of consolidation which are conspicuous on a dark red background.

Microscopic Examination.—The lung shows no change in the pleura. There is but slight thickening of the interlobular septa. The bronchi are filled with an exudate of leucocytes. The walls are somewhat thickened and infiltrated. The alveolar walls are very slightly infiltrated. They are filled with fluid and desquamated epithelial cells and with dense plugs of fibrin which are in places organized. The organization does not extend to the bronchi. Certain areas show the alveoli filled with leucocytes in a fibrin network, but these are only scattered patches. Other areas are loaded with bacteria and are necrotic, the necrosis involving the walls of the alveoli. Such bacteria are partly streptococci but partly large Gram-positive spore-bearing bacilli.

Therefore the changes are probably in part due to postmortem decomposition. Bacteriological cultures showed Gram-positive gas-producing bacilli in blood and lungs.

Case 29.—C. B. D., age 20 yrs. Began Jan. 18 with nosebleed, cold in head, and painful eyes, photophobia, fever, and chilliness. Entered hospital Jan. 23, 1918, with sore throat, reddened pharynx, no tonsillitis, a red crescentic papular eruption over face and body. Coughing, with fine râles over the entire chest, persisted. Rash lasted 5 or 6 days. Since onset patient has been hoarse and at present (Feb. 4) cannot speak above a whisper. About Jan. 30 patient developed a pain in both axillæ with marked difficulty in breathing. Râles were heard over both lungs. Inspiration lengthened and so labored as to bring in accessory muscles. Friction rub in left axilla. The percussion note later became dull or flat in the left axilla and back and the friction rub disappeared. Patient growing more and more cyanotic, conscious, and very nervous. Needle inserted at lower angle of left scapula but only blood obtained. Sputum abundant, greyish white, tenacious. Patient died on Feb. 7, 9.50 p.m., 20 days after the onset of measles. Cultures from sputum and material obtained from lung puncture showed *Streptococcus hæmolyticus*. Blood culture taken Feb. 7 negative. Autopsy Feb. 8, 9 a.m.

Anatomical Diagnosis: Clinical history of measles. Bilateral interstitial bronchopneumonia. Fibrinopurulent pleuritis (left). Early serofibrinous pericarditis.

Left pleural cavity.—Contains about 1,500 cc. of greenish brown turbid fluid. The surfaces are covered with a fibrinous exudate, but as there are numerous adhesions posteriorly most of the fluid is held in the anterior portion of the thorax. *Right pleural cavity.*—There is no excess of fluid and the surfaces are smooth anteriorly, but over the posterior part of the cavity and over the diaphragm the lung is adherent by a thin hemorrhagic fibrinous exudate. *Pericardial cavity.*—Contains about 40 cc. of slightly turbid fluid. The pericardial surfaces are slightly injected and there are a few shreds of fibrin. *Left lung.*—The lung feels flabby

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and soft but contains some firmer nodules. The upper lobe is largely air-containing while the lower is heavy, dense, and collapsed. On section the upper lobe shows very distinct interlobular septa, and in the upper posterior portion there are a few small peribronchial consolidations surrounded by grey spongy tissue. Several of these areas are embedded in the deep red tissue of each lobule. In the lower part of the lobe the consolidated portions are so numerous as to form a confluent network. Each yellowish branching nodule is bordered with red and these are separated by greyish tissue. In the lower lobe the mesial and posterior parts are thickly studded with greyish yellow areas which in places grow large and become confluent. In the outer or axillary portion of the lobe these are fewer and of smaller size. The septa are still conspicuous but the bronchi are not. The lung is covered especially over the lower part with a thick fibrinous exudate. *Right lung.*—The lung is voluminous and almost everywhere air-containing. There is a thin fibrinous exudate over the lower lobe and lower part of the upper. The bronchi are deeply reddened. The upper lobe is largely air-containing. There are a few small branched peribronchial consolidations and a large firm one 1 cm. in diameter. In the lower lobe there is no conspicuous thickening of the bronchi, but in the lowermost part the bronchi are widened and full of exudate and surrounded by feathery homogeneous, greyish red areas of consolidation. From their homogeneous uniform appearance these seem to be areas in which the alveoli are filled with exudate. There are some large opaque yellow patches and many confluent grey smooth areas. *Larynx.*—Slightly reddened and covered with mucus. No ulceration visible.

Microscopic Examination.—The tissue of the left lung shows great thickening of all the framework of the organ. The interlobular septa are wide, contain a good deal of fibrin in the form of a network, but in most places this has disappeared and the broad septum is made up of loose connective tissue with many fibroblasts. The bronchi have lost their epithelium, contain leucocytes, desquamated epithelium, and a few streptococci (Fig. 31). An effective stain reveals influenza bacilli in great numbers in bronchi and alveoli. Elastic tissue stain shows readily the original outlines, and it is clear that there is a thick layer densely infiltrated with mononuclear cells which has formed just beneath the epithelium, lifting it up. The remaining muscular and connective tissue portion of the wall is densely infiltrated with mononuclear cells and some leucocytes and is much thickened (Fig. 32). Viewed with a low power any one lobule appears denser around the central bronchus and near the surrounding interlobular septa than in the intervening zone. This is largely due to the fact that in the neighborhood of the bronchus and at the periphery near the septum the alveolar walls are greatly thickened. The epithelium is in general desquamated, but the underlying structureless membrane which can be most distinctly seen is lifted away from the capillaries which hold to the middle of the alveolar wall by a great mass of mononuclear wandering cells and newly formed connective tissue. Thus in each alveolar wall the capillaries are covered on each side by a layer of these cells

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bounded by the membrane of the wall. In the midzone of the lobule the alveolar walls are thinner. All this infiltration and new connective tissue formation forms another instance of the reason for speaking of this condition as interstitial bronchopneumonia.

The alveoli contain many desquamated epithelial cells, rather dense fibrin, and a few mononuclear wandering cells. There are few if any streptococci to be seen. But in places there are small groups of alveoli densely filled with leucocytes among which there are great numbers of streptococci. This coexistence of what may be called lobular pneumonia with the interstitial bronchopneumonia is noteworthy. The interlobular septa are composed of a network of fibroblasts (Fig. 33). The lymphatics are wide and contain a mass of cells which are practically all mononuclear. Some are as large as alveolar epithelial cells. There is often also a network of fibrin which is beginning to undergo organization. A few streptococci are found there.

In other areas of the left lung and in the right lung the inflammatory process beginning about the bronchi is associated with much edema and hemorrhage into the alveoli. The left lung shows the most extreme interstitial changes yet seen. There are quite large areas which are completely airless, the alveoli being filled with fluid and desquamated cells and blood (Fig. 34), the alveolar walls, vessels walls, and interlobular septa greatly widened by infiltration with mononuclear cells. The lymphatics are filled with mononuclears and fibrin out to the pleural exudate. The bronchi are enormously thickened and overvascularized. Usually the epithelium is lost and the thick wall densely infiltrated with mononuclears. In some places the contents of the bronchi appear to be replaced by a mass of newly formed vascular tissue.

The lobulated fat which hangs into the pleural cavity from the surface of the pericardium is covered with exudate and most of the lobules are glued together. Streptococci are abundant on the surface and extend into the ends of the open crevices but are not found in the fibrin which closes the crevices or in the tissues.

Cultures from blood, pericardial fluid, pleural fluid, and left lung reveal *Streptococcus hæmolyticus.*

Case 30.—F. E. H., age 23 yrs. Was in hospital for tonsillitis Dec. 24–29, 1917. No rash at this time. Since then has been having chills every night. On Jan. 3 developed pain in the left side of the chest and entered the hospital, Jan. 6, 1918, with signs of dulness, tubular breathing, and crepitant râles over the left lower chest. 1,000 cc. of turbid straw-colored fluid were aspirated on Jan. 21, and on Jan. 23 the left pleural cavity was drained by resection of the 7th and 8th ribs. Leucocytes 35,000. Temperature 99–104° F., pulse 90–160, respiration 20–40. Died Feb. 7, at 6 p.m. Autopsy Feb 8.

Anatomical Diagnosis: Interstitial bronchopneumonia and lobular pneumonia with abscess formation and empyema (left side). Lobular pneumonia (right lung).

Left pleural cavity.—Obliterated by fresh adhesions in the anterior portion, but posteriorly there is a cavity open to the air through an incision which interrupts

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the 7th and 8th ribs in the left anterior axillary line. This cavity contains about 400 cc. of an extremely foul greenish brown turbid fluid. The surfaces are covered where they form the wall of the cavity with a thick greenish exudate. *Right pleural cavity.*—Contains no excess of fluid and the surfaces are smooth and glistening. *Left lung.*—The lung is partly collapsed, its posterior part covered with greenish exudate. The upper lobe contains a few small consolidated areas. The lower lobe is closely studded with similar small consolidated patches which have become liquefied centrally. The intervening lung substance is collapsed and edematous. *Right lung.*—In general the lung is air-containing, but in the lower lobe there are one or two firm nodules. One of these stands out above the surrounding lung surface and the pleura over it is dull and covered with fibrinous exudate. On section this patch is opaque and yellow, but it is still possible to discern in it the bronchi filled with exudate. In other parts of the lung there are small abscess-like foci surrounded by hemorrhage.

There are evident general signs of postmortem decomposition. The skin of the abdomen is discolored and green and the gastric mucosa and retroperitoneal tissues contain large gas blebs.

Microscopic Examination.—Sections through the least affected part of the left lung show the greatly thickened pleura which is replaced by a dense granulation tissue. The bronchi are in places filled with an exudate of leucocytes and mononuclears. The adjacent alveoli show slight infiltration of the walls; the epithelial cells are desquamated and fill the lumen. Most striking is the presence of whole colonies of bacteria in the blood vessels and capillaries and sometimes in the alveoli and bronchi. Since these are present in enormous numbers in the capillaries of the liver, spleen, kidneys, and adrenals, with little or no reaction about them, it seems probable that they have become so numerous through postmortem growth. In other areas of the lung there are large patches of necrosis in which all structure is lost and merged into a granular material loaded with micrococci and masses of minute Gram-negative bacilli which may be influenza bacilli. About these there is a dense pneumonic consolidation with edema and hemorrhage in the distant margin. Many of the alveoli show a curious columnar form of epithelium which makes them look like minute bronchioles.

No cultures were made.

Case 35.—C. E. P., age 26 yrs. Entered hospital Jan. 13, 1918, complaining of pain in left chest, chills, and fever. No history of sore throat or rash. Does not remember having had measles. Dulness with tubular breathing over the left base at the back. Leucocytes 20,800. Temperature 101–105° F., pulse 120–160, respiration 30–60. Jan. 26, evidences of fluid at the left base with new signs of consolidation in upper left and lower right lobes. On Jan. 29 aspiration of the right side gave 200 cc. of cloudy reddish brown fluid. Feb. 1, severe pain in left chest. Feb. 5, rib resected on left side and drainage established after repeated aspirations during preceding 2 days. Feb. 9, patient complains of severe pains in abdomen which is greatly distended, rigid, and very tender. No special localization of tenderness. Died Feb. 10, 1918, at 10 p.m. Autopsy Feb. 11, 1918.

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Anatomical Diagnosis: Interstitial bronchopneumonia and lobular pneumonia with empyema (left). Acute pericarditis (beginning). Acute generalized peritonitis. Acute nephritis.

Upon opening the abdominal cavity there is an escape of turbid yellow fluid with flakes of fibrin. The surfaces of the peritoneum are somewhat injected on the left side but are everywhere smooth. No origin of this infection could be found in the abdominal organs. *Pericardium.*—The pericardial sac contains 50 cc. of slightly turbid greenish yellow fluid. The vessels on the inner surface of the parietal pericardium are slightly injected. *Left pleural cavity.*—There is an incision in the anterior axillary line over the 7th rib and a portion of this rib has been resected allowing fluid to escape through a rubber drainage tube. Between the collapsed lower lobe of the lung and the parietal pleura there is a cavity which contains about 400 cc. of a bloody purulent fluid. The upper lobe is adherent over its whole surface excepting a small area posteriorly where it forms part of the wall of the empyema cavity. The remaining pleural lining where it forms the wall of this cavity is covered with a fibrinopurulent exudate. *Right pleural cavity.*—Obliterated by very fresh light fibrous adhesions which are easily broken through but which bind the lung to the costal pleura and diaphragm. *Left lung.*—The pleura is much thickened and the lobes are bound together by a fibrous layer 4 mm. in thickness. The lobes are heavy and airless except at the anterior margin of the upper lobe. On section the upper lobe is dark red and rather edematous, but there are no areas of consolidation. The lower lobe is also edematous on section and reddish grey in color. The interlobular septa are prominent and in each lobule there are five or six opaque yellow areas of consolidation many of which show a central cavity or lumen. The bronchi in general are thick with reddened and edematous mucosa. The surrounding tissue is dense and yellowish. The bronchial glands are enlarged and soft. *Right lung.*—The surface is roughened and shows subpleural hemorrhages and over the inferior border of the lower lobe a thick fibrinous exudate. All the lobes are readily insufflated, although the lower was collapsed and heavy. In the upper and lower lobes and to a much less extent in the middle there are found a few small greyish translucent areas which appear to be due to thickening of the bronchioles. The bronchi are reddened. The lymph glands at the hilum are swollen and soft. *Kidneys.*—Left kidney measures 12 by 5 by 4 cm. The capsule strips readily, leaving a smooth, pale greyish, opaque surface upon which numerous small hemorrhages are to be seen. On section the cortex measures 7 mm. in width. It appears swollen and opaque. The striations are somewhat obscured by numerous small hemorrhages in the cortex. The glomeruli are visible as small greyish dots. The pyramids are dark brownish red with very distinct striations. Pelvis is normal. The right kidney is in all respects similar.

Cultures from the blood, pericardial fluid, pleural fluid, and left lung show *Streptococcus hæmolyticus* in pure culture.

Microscopic Examination.—The right lung in its lower lobe shows only rather diffuse changes which consist in the filling up of the alveoli with fluid and blood.

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The walls are not especially altered, but in the capillaries there are surprising numbers of megalocaryocytes.

Rather large bronchi shown in this section are loosely filled with leucocytes and debris of epithelium. The bronchial wall is not markedly thickened, but it is striking that in many places where the epithelium is desquamated there is a distinct adherent layer of fibrin on the wall like a diphtheritic membrane.

The left lung, covered with a thick vascular layer of granulation tissue surrounded by fibrin, is atelectatic, and the bronchi contain bacteria and pus. There are no other remarkable alterations in this part of the lung. But in the lower lobe the changes are advanced. The pleura is as just described. The interlobular septa are wide and dense and contain lymphatics plugged with clots made up of fibrin, leucocytes, and bacteria. The bronchi are dilated, the walls greatly thickened by mononuclear infiltration, the epithelium is desquamated, and the lumen filled with this and a mixture of fluid and leucocytes with bacteria. Influenza bacilli are present in numbers among the streptococci. From the region of the bronchi the alveolar walls are thickened by infiltration with mononuclear cells and a great many leucocytes, but at a little distance this thickening disappears. The whole tissue is compact and solid because each alveolus while partly collapsed contains desquamated epithelium, fluid, and blood. There are not many mononuclear cells in the alveoli, but even in outlying places they persist in the walls of the small blood vessels and adjacent alveoli.

There are many patches of lobular consolidation in which the alveoli are tightly packed with leucocytes, which in places are entirely disintegrated and appear as a dust of nuclear fragments. They are often surrounded by wide zones of hemorrhage. These are areas of lobular pneumonia rich in bacteria, but in contrast there are often found minute bronchioles which are filled with leucocytes and whose walls are greatly widened by infiltration of mononuclears and rendered so indefinite that their outlines cannot easily be recognized either within or without.

The kidney shows very little change in the glomeruli. There is occasionally some coagulated fluid in the capsule. Epithelium of the tubules much degenerated and partly desquamated. The tubules are in places filled with blood and leucocytes. There are a few leucocytes in the interstitial tissue.

Case 58.—M. F. M., age 25 yrs. History negative. Present illness began on Jan. 10, 1918, with a severe cold accompanied by sore throat, headache, and fever. Began to have pain in his left side on the day of admission to the hospital, Jan. 13. Dulness was found over both lower lobes but there were no râles and breath sounds were faint. Temperature ranged from 101–104.8° F., pulse 120–130, and respiration 28–48 until Jan. 28, when temperature fell to normal. There was marked delirium on Jan. 18. Pus was aspirated from the right chest on Jan. 27, and the next day the 7th rib was resected and the right pleura drained. The temperature remained rather high, 100–102°, and the patient was occasionally delirious until his death on Mar. 8, 1918. Autopsy Mar. 8, 1918.

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Anatomical Diagnosis: Old interstitial bronchopneumonia with empyema (right). Abscess of lung. Acute peritonitis.

Left pleural cavity.—Contains no fluid but there are light fibrinous adhesions on the back of each lobe. The lower lobe is adherent to the diaphragm and there are slight fibrinous adhesions on the anterior margin of both lobes. *Right pleural cavity.*—In the right anterior axillary line there is a large operative wound over the 6th rib. The margins are covered with granulation tissue and a large piece of the underlying rib has been resected. The lung can be seen to be collapsed. The pleural surfaces are thickened and reddened and covered with a soft fibrinopurulent exudate which overlies a layer of granulation tissue. The cavity contains about 300 cc. of very foul pus. *Left lung.*—The whole lung can be inflated artificially and on section is found to be air-containing everywhere with the exception of a few areas in the lower posterior portion of the upper lobe and a few in the lower lobe. These are grouped together, two and three being found in each lobule. They have a central lumen which is filled with a yellow purulent fluid, and are surrounded by a hemorrhagic zone. The bronchi contain a sticky mucoid material, and the mucosa is hemorrhagic. The interlobular septa are not thickened. Bronchial glands only slightly enlarged. *Right lung.*—Completely collapsed and pressed against the vertebral column. It is densely adherent to the diaphragm by fibrous adhesions. Over the anterior surface of the upper lobe is a large necrotic area, irregular in form and measuring 8 by 6 cm. which is covered by dirty, foul smelling, greenish yellow exudate. On section this mass replaces about half the upper lobe. Its central part is softened, very foul, and yellowish green in color, and this condition radiates out into the surrounding lung substance. The rest of the upper lobe is airless, dark grey, and rather granular in appearance. There are numerous thickened edematous interlobular septa, and in the lobules so outlined the branches of the small bronchi filled with yellow exudate are prominent. One such group in the posterior part of the lobe is surrounded by a hemorrhagic zone. The lower lobe is also heavy, airless, and flabby. In the posterior part there are several lobules which are pale grey and quite airless, in which there are peribronchial nodules. These lobules are sharply outlined by the interlobular septa. *Pericardium.*—Contains 30 cc. of turbid fluid with floating shreds of fibrin. The pericardial surfaces are, however, still glossy. Heart is normal.

Culture from the blood gave a Gram-positive streptococcus, but this was overgrown by putrefactive bacilli.

Microscopic Examination.—The pleura over the right lung is extremely thick and dense with radially placed blood vessels and an overlying layer of fibrin on the surface of which are great quantities of bacteria.

Most of the sections show wide and rather dense interlobular septa running into the lung substance. Most of the fibrin and fluid in these are absorbed and only remnants of dense red-staining fibrin remain. The lymphatics are

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hard to find, but where they can be outlined they are distended with a mass of new connective tissue infiltrated with cells. Evidently the thrombi with abundant leucocytes and bacteria have in this case been organized in the same way as the contents of the alveoli and replaced by connective tissue. The septa themselves are composed of rather dense fibrous tissue with many wandering cells.

The bronchi retain their epithelium and are filled with leucocytes in most cases, but their walls are greatly thickened and have the appearance of a layer of granulation tissue with abundant wide blood vessels running radially. They are densely infiltrated with wandering mononuclear cells. The alveolar walls are similarly thickened. Over large areas they are quite collapsed. In others they contain dense fibrin which is often in an advanced stage of organization. Most of them contain fluid and abundant desquamated epithelial cells. There are areas too in which these changes are not developed but in which the bronchi and alveolar walls remain thin and the alveoli are filled with fluid and with polymorphonuclear leucocytes.

In the districts in which the alveoli and bronchi are most thickened there are large irregular abscesses which send off long prolongations and are marked out by a dense wall of fibrin with fragmented nuclei. Within these walls the whole substance of the lung has been broken down, shreds of elastic tissue remain, but the rest is seen in the form of a necrotic debris with great numbers of bacteria. It is not possible to maintain in this case that the formation of such an abscess occurs only in an area of lobular pneumonia; on the other hand the areas of leucocytic exudate show none of the abscesses.

One receives the impression that this is a protracted case of interstitial bronchopneumonia lengthened in its course by the persistence of the empyema and that in some senses an advance toward healing has occurred, especially in the organization of the exudate in alveoli and lymphatics. But the occurrence of large abscesses has interfered with the completion of this process. The whole arrangement of the lymphatics must be greatly altered by such a process, and if recovery had occurred new lymphatics must have been required.

Case 176.—A. G., age 24 yrs. Began on Mar. 25, 1918, with measles. On Apr. 6 complained of pain in the right side, and physical examination on Apr. 10 resulted in the diagnosis of lobar pneumonia involving the right lower and middle lobes. On Apr. 11 empyema was recognized on the right side and an operation was performed with resection of the 9th rib and drainage of the pleural cavity. Died May 9, 1918, at 6 a.m. The clinical diagnosis at the time of death was lobar pneumonia, the right lower lobe resolving. Bronchopneumonia (left); bilateral empyema. Acute pericarditis and myocarditis. Culture from the blood on Apr. 28 was sterile. On Apr. 11 culture from the pleural exudate gave *Streptococcus hæmolyticus*. Autopsy May 9, 1918, at 11 a.m.

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Anatomical Diagnosis: Clinical history of measles. Lobular pneumonia (right) with old empyema. Fresh fibrinopurulent pleuritis (left). Subacute purulent pericarditis with adhesions. Acute serofibrinous peritonitis. Phlegmonous infiltration of neck.

Left pleural cavity.—Contains 500 cc. of thick turbid, slightly blood-stained brownish fluid. The costal pleura is covered with yellow fibrin which overlies a velvety red pleural membrane. The lung is plastered against the pericardium and is adherent along the vertebral column to its apex. Otherwise it is everywhere free, but the fibrin is especially thick between the lung and diaphragm. *Right pleural cavity.*—In the right back 3 cm. below the angle of the scapula there is a wound about 7 cm. long rising in an oblique direction along the line of the 9th rib. The ends of the rib project through the granulating wound. The pleural cavity is free from adhesions anteriorly from apex to diaphragm, back to the midaxillary line where it is obliterated above the 6th rib by adhesions, and below that level opens out into a large cavity which extends back to the vertebral column. This space is lined with granulation tissue and fibrin and into it the wound in the back opens. *Pericardial sac.*—Greatly thickened. The anterior wall is fully 6 mm. in thickness and is lined with a layer of translucent tissue about 4 mm. thick which contains opacities. The cavity is partially obliterated, but the remaining space contains about 40 cc. of thick creamy pus which is pale greenish yellow in color and contains thick clumps of yellow fibrinous material. *Peritoneal surfaces.*—Have lost their gloss to some extent and there is some turbid fluid with flakes of fibrin in various dependent parts. *Left lung.*—Almost entirely collapsed and blue and flabby. The whole lung can be inflated and on section presents a normal texture without consolidation and with practically normal bronchi. There is a small part of the lower lobe posteriorly which fails to become inflated. *Right lung.*—The surface is changed in appearance by the alterations of the pleura already described. The bronchial glands are enlarged and opaque grey in color. The upper lobe contains air throughout; it is normal in texture and there are no areas of consolidation. The middle lobe is partly atelectatic but nowhere consolidated. The lower lobe contains air in its upper part, but the lower part is collapsed. In this collapsed part there is a group of small areas of consolidation which are grey on a greyish red background, more or less confluent and irregular in outline. They seem not distinctly peribronchial, but to consist of alveoli filled with exudate. In the more posterior part of the lobe there are even more distinct grey areas of consolidation in which plugs of exudate can be seen in each alveolus. The bronchi and blood vessels are not thickened, but the interlobular septa are rather prominent. *Tonsils, larynx, and pharynx.*—Fairly normal. There is a multilocular abscess in the intermuscular spaces of the left side of the neck extending up as far as the mastoid with which it has no apparent connection and down behind the clavicle to the pleura with which it does not communicate. The right shoulder joint is in-

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tact, but the abscess extends between the scapula and the vertebral ends of the upper ribs for a long distance.

Cultures from both lungs, left pleura, pericardium, and from the abscess in the neck gave *Streptococcus hæmolyticus*. Culture from the heart's blood was sterile.

Microscopic Examination.—The substance of the lower lobe of the right lung presents the only remarkable change. The pleura is greatly thickened and converted into a rather dense granulation tissue with overlying fibrin. The interlobular septa are extraordinarily wide and rather dense. They appear to represent old changes. The lymphatics which run in these are distended with cells which are partly leucocytes, partly mononuclear cells, and this material is loaded with Gram-positive cocci which are far more numerous here than elsewhere. They are usually in pairs and only rarely in longer chains. The bronchi are slightly thickened and their walls moderately infiltrated with cells which are in part polymorphonuclear leucocytes. They contain a purulent exudate which is full of streptococci. No influenza bacilli are found. The alveolar walls are slightly thickened, in many places not at all. They are infiltrated in places with leucocytes, but near the blood vessels they may be filled with mononuclear cells. On the basis of this rather slight interstitial change there is a distinct intra-alveolar exudate of red corpuscles, leucocytes in great numbers, and fibrin. It constitutes a definite lobular pneumonia. The bacteria are present among the polymorphonuclear leucocytes, but not in great numbers and not more distinctly in chains than elsewhere. In the margin or tip of the lower lobe there is a peculiar change. The interstitial tissue is greatly increased and infiltrated with leucocytes and fibrin. The alveoli appear as rather widely separated spaces in this tissue and either have no lining or are lined with thin scale-like epithelium. The bronchioles with their columnar epithelium similarly appear isolated in the dense tissue.

Sections of the connective tissue and muscle about the abscess of the neck show great numbers of streptococci in necrotic tissue and in the crevices of a diffuse granulation tissue.

Case 181.—E. J., age 26 yrs. Began Mar. 24, 1918, with bronchitis. Onset rather sudden with chills, fever, headache, weakness, and general malaise. Scattered râles heard over lungs. On Mar. 31 subcrepitant râles and bronchial breathing over the left lower lobe posteriorly. On Apr. 1 a small area of consolidation in the right lower lobe in the axillary line. On Apr. 16 no definite signs over the lungs. Aspiration of right axilla negative. Apr. 19, suppurative otitis. Crepitant râles and slightly diminished resonance over whole right side anteriorly. Apr. 21, impaired breathing over right lower lobe. Apr. 26, 200 cc. of limpid greenish yellow fluid aspirated from right upper chest. This fluid contained *Streptococcus hæmolyticus* as shown by culture. Flatness over this region next day. May 5, aspirated 300 cc. from right chest. Culture from pleural fluid on May 10 gave *Streptococcus hæmolyticus*. Died May 10, 1918, at 2.15 p.m. Autopsy May 11, 1918, at 10 a.m.

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Anatomical Diagnosis: Interstitial bronchopneumonia (bilateral) with abscess formation and empyema (right). Lobular pneumonia (left).

Left pleural cavity.—Contains no fluid. Surfaces smooth. *Right pleural cavity.*—Contains 400 cc. of thick greenish mixture of fibrin and pus which will hardly pour. The right lung is plastered against the pericardial sac. The apical part of the lung is adherent along the 3rd rib laterally, but otherwise the pleural surfaces are held apart. They are covered with a thick yellowish shaggy layer of fibrin. *Left lung.*—The lung is voluminous with smooth, glistening surfaces, but some small nodules can be felt in its substance. The upper lobe is easily inflated and on section is normal in texture. The lower lobe is also easily distended, but posteriorly and below there are some small greyish yellow nodular consolidations. *Right lung.*—The organ is collapsed, pasty, and heavy, and one may palpate nodular consolidations in its substance. On section there is found a cavity about 3 cm. in diameter in the substance of the upper lobe (Fig. 35). This excavation is full of purulent material and is in open communication with a large bronchus whose walls it has abruptly interrupted. There is no communication with the pleural space. The lung tissue surrounding this cavity is irregularly consolidated. The interlobular septa are conspicuous. The lower lobe shows the bronchi widely dilated to the periphery and filled with purulent material. About these there are areas of consolidation which become confluent so that practically the whole posterior part of the lower lobe is airless, the smooth firm areas being separated in places by only a narrow line of air-containing tissue. *Pharynx and larynx.*—The pharynx is not especially reddened. The larynx including epiglottis and vocal cords is pale, smooth, and normal throughout. The mucosa of the trachea is pale.

Cultures made at autopsy show *Streptococcus hæmolyticus* in the heart's blood, both lungs, and right pleura.

Microscopic Examination.—The left lung shows a thin smooth pleura. The interlobular septa are not thickened and the lymphatics are inconspicuous. There is a widespread filling of the bronchioles with purulent exudate. The walls are moderately thickened and hyperemic and infiltrated with mononuclear cells. This alteration is relatively slight, however, and the corresponding changes in the adjacent alveolar walls are also very slight. Still there are areas about many of these bronchi in which the alveoli are filled with thick fluid, with blood, and desquamated epithelial cells. Most of the bronchi are surrounded, however, by small groups of alveoli which contain a dense exudate of leucocytes with delicate network of fibrin and very little blood. There are many streptococci among these leucocytes, and numerous influenza bacilli.

The right lung shows a thick pleura covered with granulation tissue and fibrin. The interlobular septa and indeed all the connective tissue structures throughout the lung are enormously thickened and rendered dense by a new growth of tissue.

The bronchi are greatly distended and filled with a solid mass of leucocytes. Their walls still show in most places the layer of epithelium, but some of them

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are completely denuded. In general the bronchial walls are greatly thickened and converted into a vascular granulation tissue which is densely infiltrated with mononuclear cells. The alveoli are practically all collapsed, their walls greatly thickened and infiltrated, but there is not much beyond a few alveolar epithelial cells in their cavities. The lymphatics are nowhere conspicuous, and many of them have probably been obliterated.

This case exhibits, therefore, an old interstitial bronchopneumonia with great dilatation of the bronchi and induration of the framework of the lung, with empyema causing a collapse, and necrosis and cavity formation in the upper lobe. All this affects the right lung while the left lung is studded with patches of lobular pneumonia in a tissue in which there are traces of the interstitial process.

Case 194.—J. J., age 25 yrs. Negro. Had measles on May 3, 1918. On admission, May 9, râles at both bases. Lobar pneumonia of right lower lobe recognized May 10, 1918. May 13, dulness of right lower lobe with râles; hoarseness. On May 16 fluid was suspected in the right chest and peritonitis was also diagnosed. Right lower lobe very dull; breath sounds distant. Sputum on May 13 was yellow, mucopurulent, and contained Gram-positive cocci which proved to be *Staphylococcus aureus* and *Streptococcus hæmolyticus*. Influenza bacilli were also there. Died May 16, 1918, at 1 p.m. Autopsy May 16, 1918, 2 hours after death.

Anatomical Diagnosis: Early interstitial bronchopneumonia (left), with lobular pneumonia. Empyema with collapse of lung (right). Acute fibrinopurulent peritonitis. Acute splenic tumor with hemorrhagic infarctions. Ulcerative laryngitis.

Peritoneum.—Contains a yellow fluid with flakes of fibrin which is plastered on the abdominal organs. The pelvis contains a purulent fluid. *Left pleural cavity.*—Contains no excess of fluid, but the surfaces are roughened by a fresh fibrinous exudate. *Right pleural cavity.*—This side contains a great deal (2.5 liters) of turbid fluid much of which is imprisoned in a space between the lung, diaphragm, and pericardial sac. The fluid is brownish and turbid with a thick sediment. *Left lung.*—The lung is voluminous (Fig. 36). The surfaces are smooth except at the posterior part of the lower lobe where the pleura is deep purplish and covers an area which is firm and nodular. The upper lobe is air-containing throughout and normal in texture. The bronchi are not altered. The lower lobe is thickly studded with small greyish nodules which correspond with the terminations of the bronchi and are surrounded by bright red hemorrhagic areas. In the lower posterior part of the lobe there are confluent hemorrhages within which there are several dry, opaque, dull red patches which stand up a little above the surface. The bronchi are widened a little and contain a bloody, frothy, grey exudate. Their walls are deeply congested. The bronchial glands are greatly enlarged, edematous, and grey. *Right lung.*—The right lung is collapsed into a wrinkled soft mass. The lobes are somewhat adherent, and on pulling them apart small cavities in the fibrin, containing green pus, are torn open. The lung can be artificially inflated and then on section the whole lung

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is found to be air-containing. The cut surface is smooth and satiny. The bronchi are reddened and contain only frothy fluid. The bronchial glands are large. *Pharynx and larynx.*—Tonsils not enlarged. Epiglottis is pale. The vocal cords are distinctly ulcerated along their edges, but the rest of the larynx seems normal. *Spleen.*—Enlarged, measuring 16.5 by 12.5 by 5 cm. It is irregular in consistency and on section there are dark red, dry looking areas which are firmer than the rest and extend deep into the spleen. It is impossible to make out any plugs in the vessels; in fact liquid blood can be squeezed from the vessels in the centers of these areas. The Malpighian bodies are pretty well seen throughout the cut surface.

Cultures made at autopsy showed *Streptococcus hæmolyticus* in the heart's blood, right and left lung, right pleura, and peritoneum. The streptococci were mixed with many other organisms in the smear from the ulcer of the vocal cord. The right lung gave also *Staphylococcus aureus.*

Microscopic Examination.—The diaphragm shows an exudate of fibrin and leucocytes on both sides. That on the pleural surface is dense and compact while that on the peritoneal side is very loose. The absorbent lymphatics in the peritoneal surface are packed with leucocytes and such dense thrombi can be tracked into the larger lymphatics which extend to the pleural surface. It seems probable that the infection is transmitted from pleura to peritoneum by way of the lymphatics against the ordinary course of their stream which becomes possible when they are thus obstructed by a thrombus in which the bacteria are growing. It is analogous to the condition in the lung which leads to empyema.

In the left lung most of the tissue is properly air-containing, but there are scattered bronchi which contain purulent or bloody exudate whose walls are thickened and infiltrated. They are surrounded by a group of alveoli whose walls are similarly infiltrated, while their cavities are filled with leucocytes or desquamated epithelial cells. They together with the adjacent alveoli contain a great quantity of blood. Some of these patches are overwhelmingly filled with blood so that it is difficult to see anything else, while others have the alveoli filled entirely with polymorphonuclear leucocytes. The latter places are loaded with streptococci which are much more numerous there than in the more intensely hemorrhagic patches. There are also some rather large Gram-positive bacilli in the affected parts of the tissue and these are found in numbers in the hemorrhagic areas. The dull red dry patch in the lower part of the lobe is found on section to be in large part necrotic. The nuclei of the alveolar walls no longer stain, but the walls are yet traceable through the solid mass of blood. The capillaries can be seen to be much distended. The bronchi are widened and thickened by infiltration and contain streptococci, although there are not many organisms in the hemorrhagic tissue. The blood vessels contain dense clots, but they have not definitely the architecture of thrombi. All the alveoli in this neighborhood contain some leucocytes, but there are regions in which their cavities are closely packed with leucocytes among which streptococci are found.

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The right lung shows practically no alteration of the tissue. The bronchi are thin walled and not infiltrated. The pleura is, however, thickened by the formation of a granulation tissue and the section shows one of the interlobar encapsulated pockets which is lined with a thickened pleura and fibrin in the same way. The immediately adjacent tissue is still collapsed and perhaps somewhat indurated.

Case 205.—H. W., age 29 yrs. Negro. Began on May 4, 1918, with measles. Later was transferred to pneumonia ward with signs of bronchopneumonia involving both lungs on May 7, 1918. Sputum contained *Streptococcus hæmolyticus* and influenza bacillus. Blood culture on May 8 was sterile. On May 15 otitis media developed in both ears and the patient became very deaf. Died May 20, 1918, at 5.50 p.m. Autopsy May 21, 1918.

Anatomical Diagnosis: Interstitial bronchopneumonia and lobular pneumonia (bilateral). Empyema (right). Bilateral symmetrical rupture of rectus abdominis. Suppurative otitis media (bilateral).

On incision through the anterior abdominal wall a cavity is found in the rectus abdominis at the junction of the lower and middle third of the muscle. This is due to a rupture of the muscle which leaves a space 4 cm. in diameter filled with a bloody fluid. There is a similar hemorrhagic cavity in the opposite muscle at exactly the same level (Fig. 37). On section the ends of the muscle are deeply infiltrated with blood and are dark red and opaque. The lower fragment is distinctly yellow. The hemorrhages bulge into the peritoneal cavity and fluctuate, but there is no excess of fluid in that cavity nor any hemorrhage, and the peritoneal surface of the bulging masses is smooth. *Left pleural cavity.*—Contains no excess of fluid. The surfaces are smooth. *Right pleural cavity.*—The cavity contains 400 cc. of turbid brownish fluid in which float flakes of fibrin. The surface of the lung is gelatinous and covered thickly with slimy patches of fibrin. There are a few small hemorrhages. *Left lung.*—The lung is voluminous and appears to contain some air everywhere. It is readily inflated artificially. On section the upper lobe is found to contain numerous small nodular areas of grey consolidation not especially surrounded by hemorrhage but apparently surrounding the terminal parts of the bronchi. They measure 2 to 6 mm. in diameter and become more numerous in the posterior part of the lobe. They are nowhere confluent. In the lower lobe the same condition exists and the nodules are extremely numerous in the posterior part of the lobe (Fig. 38). *Right lung.*—The lung is heavy and pasty and dark reddish purple in color. The bronchial glands at the hilum are very much enlarged. The pleural surface is roughened by fibrin. The anterior portions of the upper and middle lobes are air-containing. The posterior portions and the lower lobe are collapsed. On section the whole lung is thickly studded with grey peribronchial nodules becoming more abundant in the posterior parts. The interlobular septa are prominent, marking out the lobules, and each lobule contains several nodules. There is in the lower lobe a large wedge-shaped area running back to the posterior border in which the nodules are not

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surrounded by air-containing tissue but are broad and confluent forming a greyish red area in which more opaque yellow patches are visible (Fig. 39). The bronchi are dilated and their mucosa is reddened. *Pharynx and larynx.*—The posterior nares and pharynx are reddened. The tonsils are normal. The vocal cords are rather deeply ulcerated throughout most of their length. The mucosa of the trachea is reddened. *Middle ear.*—On exposing the cavities both middle ears are found to be filled with pus.

Cultures at autopsy showed *Streptococcus hæmolyticus* in the heart's blood, both lungs, and right pleura, also in the right middle ear, but the bloody fluid from the ruptured rectus abdominis gave no growth.

Microscopic Examination.—The conditions found throughout the two lungs are about the same.

The pleura is thick on the right side and covered with rather homogeneous fibrin. The interlobular septa are as a rule not very conspicuous, but some of them contain large lymphatics distended with a mass of leucocytes which are usually almost necrotic and disintegrated into a poorly staining debris.

The bronchi are filled with a similar mass of granular and fragmented leucocytes containing streptococci and influenza bacilli. The walls are greatly thickened, hyperemic, and densely infiltrated with mononuclear cells. In most places the epithelium has been destroyed and a necrotic layer forms the lining. The surrounding tissue is edematous, but the nearby alveoli are filled with desquamated epithelial cells, mononuclear wandering cells, blood, and leucocytes. In places the leucocytes predominate and produce patches of what would be recognized as a lobular exudative pneumonia. Here, too, the leucocytes are much disintegrated. But in most places this exudative type is not found and the lesion is essentially that so often described as interstitial bronchopneumonia. The thickening of the alveolar walls is relatively slight, but the lining epithelium tends to be cubical and is evidently in proliferation.

The rectus abdominis muscle shows a mass of blood clot in contact with the ruptured end where necrotic hyaline muscle tissue alone is found. All through the muscle, however, in diminishing degree as one passes away from the point of the rupture there are extreme alterations which consist in the conversion of the muscle fibers into hyaline material. This looks like an old process. Each clump is surrounded by a mass of nuclei which are probably sarcolemma nuclei which have been concentrated. In places these look like wandering cells, but they are fairly well limited to the surrounding sheath of each hyaline clump. A separate and more detailed study of these muscular changes must be made.

This group of cases is not sharply distinguished from the preceding, since many of those showed a few foci of lobular pneumonia, but it is separated because it is desired to show that this combination is possible in an advanced degree. It may possibly represent a stage in the whole process at which the lung which is the seat of a lesion in the

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production of which the tissues have evinced a marked power of resistance finally fails so that the organisms invade more readily. But not much stress can be laid upon this suggestion since these lesions seem to develop side by side in some cases of brief duration.

Dr. Allen Krause has suggested that in a person already tuberculous the sudden appearance of a tuberculous pneumonia is probably due to hypersensitization of the individual by the old tuberculosis, so that the introduction of bacteria into a fresh bronchus results in pneumonic infiltration in a way that could not happen in a normal non-sensitized person. It seems possible that this suggestion might be transferred to the case of this combined form of streptococcal pneumonia. We have observed the anatomical difference between the lesions and especially the type of distribution of bacteria in the two forms and have found that in a lung in which in general the streptococci are limited to bronchi and lymphatics there suddenly appear patches in which the alveoli are filled with bacteria and with leucocytes which tend to act toward them as phagocytes. We have spoken of this as a final failure of resistance—possibly the failure of resistance has through the action of the poison of the original infection become an actual welcome to the invaders.

In Cases 181, 205, and 29 there were influenza bacilli in the bronchial exudate. These must be looked upon as possible participants in the production of the interstitial changes. Indeed, except for the occurrence of advanced lesions of this type in cases in which the streptococcus is present alone (Nos. 34, 41, 178, and 184), it would be difficult to insist that the influenza bacillus is not regularly the cause of the interstitial changes.

In its gross appearance such a lung resembles closely those just described. Nevertheless one may recognize here and there on the cut surface irregularly outlined areas which are solid, dull and opaque, and rather dry looking, grey or greyish red, and generally accompanied by a wide zone of hemorrhage. Such areas can be seen in the lungs of Cases 194, 184, 178, and others.

On microscopic examination these prove to be areas in which the interstitial changes described before which lead to the thickening of the alveolar walls are absent. Thickened bronchi and widened interlobular septa may pass nearby, but in these areas the alveoli are thin

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walled and widely distended or packed with an exudate which is composed chiefly of polymorphonuclear leucocytes in a delicate network of fibrin. Blood corpuscles are present in small numbers and in far greater numbers in the adjoining or marginal alveoli. The most interesting feature is found in the distribution of the streptococci which are present in great numbers all through the exudate, usually in pairs or short chains or even singly. They lie everywhere among the leucocytes, often within some of the cells which have acted as phagocytes, but usually free. It is noteworthy that in most of these cases the leucocytes forming the exudate in the alveoli show signs of disintegration. In places their nuclei stain indefinitely or are fragmented and the outlines of the cells have become extremely indistinct. In some cases, as in No. 194, there are areas of necrosis involving the alveolar walls and surrounded by hemorrhage.

Other areas of lobular consolidation containing the streptococci in numbers are surrounded by zones of edema in which the alveoli contain only fluid in which float a few chains of streptococci.

These cases show also peculiarly well the lesions of the interstitial bronchopneumonia, sometimes very fresh as in Cases 178 and 184, sometimes old as in Cases 29, 58, and 181. In the last of these, No. 181, there is extensive bronchiectasis in the lower lobe and a cavity in communication with a bronchus in the upper lobe of one lung, while the opposite lung is studded with foci of lobular pneumonia together with the fresher stages of the interstitial change in the bronchi.

Such lobular lesions appear, however, in their most destructive form in the third group of cases in which they are not combined with the interstitial changes.

3. Lobular Pneumonia.

Case 20.—J. C., age 22 yrs. Entered hospital Jan. 28, 1918, complaining of headache, rash, and pain in the eyes. Symptoms of 8 hours duration. Very faint papular rash on chest, arms, and face. Conjunctivæ injected, pharynx red, Koplik's spots present. No dulness, but fine moist râles throughout both lungs. Temperature 101–106° F., pulse 100–140, respiration 20–50. Died Feb. 4. Autopsy 2 hours later.

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Anatomical Diagnosis: Confluent lobular pneumonia with abscess formation. Hemorrhagic serofibrinous pleuritis. Hemorrhagic lobular pneumonia (left lung).

Left pleural cavity.—Contains no excess of fluid and the surfaces are smooth and glistening. *Right pleural cavity.*—Contains about 1,500 cc. of turbid greenish fluid with some floating fibrin. The surface of the right lung is red and dull looking, and this appearance seen also on the parietal pleura is due to intense injection of the blood vessels and minute hemorrhages. There is very little deposit of fibrin. The lung is much collapsed but floats upon the surface of the fluid. *Left lung.*—Very voluminous with smooth surface but mottled posteriorly with dark red platelets. It is somewhat collapsed. The anterior portion is air-containing, the posterior portion thickly studded with slightly elevated dry hemorrhagic patches from 2 to 5 mm. in diameter. In these areas there is no very definite consolidation, there is no yellow opacity nor any solid nodule, nor can distinct alveolar plugs of exudate be seen. Bronchi are not definitely seen in the centers. *Right lung (Fig. 40).*—Adherent to a slight degree. It is almost entirely collapsed. In the posterior part of the lower lobe there is a large solid mass about 8 cm. in diameter, which is seen through the pleura to be purplish black in color. There are a few small rounded or branched opaque yellow areas which shine through. On section the lung is very deep red throughout, but the firm area in the lower lobe is almost black and a quantity of turbid bloody fluid exudes from it. In the upper lobe which is fairly easily insufflated there are many small irregular patches of grey consolidation in which each alveolus contains a plug of exudate. These are dull brownish grey, dry, and hemorrhagic. In the lower lobe there are many confluent areas of this sort often showing central bronchioles. They are greyish red and the intervening lung is hemorrhagic and solid. Each blood vessel is sheathed in a great wide mantle of yellowish white suggesting distension of the adventitial lymphatics with purulent exudate. Toward the lower margin such beaded yellow strands run out in the interlobular septa to the pleura where they spread out as yellow networks immediately under the surface. Some are quite large and in the depth of the lung show softened centers like abscesses. There is no fibrinous exudate on the surface. Bronchial glands slightly enlarged with some pigmentation.

Microscopic Examination.—The left lung shows early hemorrhagic patches. In these the central bronchiole and the adjacent alveoli contain streptococci in long chains and in great numbers. There is a fresh exudate of leucocytes with abundant red corpuscles but little fibrin. This intensely hemorrhagic exudate with few leucocytes and little fibrin is characteristic of all the patches.

The right lung shows much edema and a leucocytic exudate in the alveoli. The lymphatics are distended with exudate and here and elsewhere there are myriads of streptococci. In places there are actual abscesses into which the alveolar walls project and end abruptly. These abscesses are loaded with streptococci. The bronchial and blood vessel walls are infiltrated with leucocytes and some mononuclear cells. The lower lobe of the right lung shows large

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areas in which the alveolar walls are necrotic and their cavities filled with necrotic material which is loaded with streptococci in long chains. All the surrounding alveoli are packed with red corpuscles with rather few leucocytes and little fibrin. The bronchi in the neighborhood are also full of leucocytes and bacteria, their walls are infiltrated with mononuclears and leucocytes, and markedly thickened. The lymphatics are distended with exudate. Streptococci are present everywhere in pure culture and are in long chains of 20 to 30 elements. They have about them a pink-staining material which is ragged and irregular in outline, like adhering albuminous material. Where there is much fibrin there are no organisms; on the contrary they are especially numerous in the necrotic areas.

Cultures from right and left lung show *Streptococcus hæmolyticus*.

The impression gained from this case is that the individual offered no resistance to the virulent infection, so that while in the left lung there are patches of lobular pneumonia in its early stages, the right shows extensive areas of necrosis with hemorrhage and little reaction.

Case 26.—D. C. H., age 21 yrs. Began Jan. 20, 1918, with photophobia, sore throat, fever, and headache. Entered hospital Jan. 25 with conjunctivitis, reddened throat, Koplik's spots, and red papular rash over entire body. Jan. 30, developed cough and profuse expectoration; râles over entire chest. Temperature 98–104° F., pulse 70–150, respiration 15–50. On Feb. 4 and 5 marked dulness over lower left chest. Flatness over left back on Feb. 6. Abundant râles everywhere in both lungs. Died Feb. 7, 5.30 a.m. Cultures from sputum showed *Streptococcus hæmolyticus* in almost pure state.

Summary of Clinical History.—(Dr. R. Cole.) The signs were those of diffuse pulmonary involvement, especially at the left base, and suggested consolidation rather than fluid. Breath sounds over this area were loud and tubular. Whispered voice sounds well transmitted and the tactile fremitus well felt. The percussion note over this area was very dull, practically flat. The presence of fluid was suspected, although the signs were not definite. Autopsy Feb. 7, 10.45 a.m.

Anatomical Diagnosis: Confluent lobular pneumonia. Serofibrinous pleuritis. Atelectasis of lung. Pericardial ecchymoses.

Left pleural cavity.—Obliterated anteriorly by fresh fibrinous adhesions, but in the posterior part it contains 1,200 cc. of turbid greenish fluid with shreds of fibrin. The pleural surfaces are covered with a thick shaggy exudate of fibrin. *Right pleural cavity.*—Contains no excess of fluid, but the surfaces have lost their gloss and are roughened by a very thin exudate of fibrin in patches. *Left lung (Fig. 41).*—There is a thick pleural exudate of fibrin, the underlying pleura being slightly thickened. The lung is flabby and airless except in the anterior margin of the lobes, but on artificial insufflation only the superficial portion of the lower lobe remains collapsed. There are some patches of spongy grey tissue alternating with the generally red lung substance. No areas of actual consolidation are visible. The bronchi seem relatively little changed, but

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many of the blood vessels are sheathed in thick yellowish white mantles which shine through the overlying tissue and appear to be due to an infiltration of their adventitia or the distension of the lymphatics in their walls. Bronchial glands are slightly enlarged. *Right lung.*—Very voluminous and mottled with alternating emphysematous and collapsed areas. In the upper lobe there is an area of homogeneous consolidation with alveoli filled with exudate. In the more posterior part of this lobe there are several small grey foci about 1 mm. in diameter which project slightly. So too in the middle lobe there are several areas of consolidation involving two or three lobules. Elsewhere and throughout the lower lobe there is no consolidation. *Pericardium.*—There are many minute hemorrhages in the epicardium and in the parietal pericardium. The pericardial sac contains about 50 cc. of fluid which is not turbid but contains floating shreds of fibrin. Pericardial surfaces are glistening.

Microscopic Examination.—Section through the right lung including the pleura and the margin of one of the sharply outlined areas of consolidation shows that the pleura is covered with fibrin which is thickly sprinkled with streptococci. The interlobular septa are very wide and edematous and enclose a network of fibrin, but this is especially true of the deeper portions and the adventitia of the larger vessels. The bronchi are distinctly but slightly thickened and infiltrated with mononuclear cells. They contain polymorphonuclear leucocytes. The alveolar walls are not thickened or infiltrated. In some areas the alveoli contain coagulated fluid with desquamated epithelial cells. In other rather sharply outlined patches they contain packed leucocytes. All these alveoli are found to contain great numbers of streptococci in pairs or short twisted chains. No other bacteria are found. There is practically no fibrin. The streptococci are very numerous in the substance of the pleura and in the lymphatics there, and can be traced through to the fibrinous exudate.

The uniform consolidation of certain whole lobules is much like that in lobar pneumonia. Polymorphonuclear leucocytes are densely crowded in the alveoli, but there is little fibrin and few red corpuscles. The alveolar capillaries have a hyaline appearance as though the corpuscles had fused.

Sections of the left lung show the very thick layer of granulation tissue covered by a thick layer of fibrin which represents the lining of the empyema cavity. From this, greatly widened interlobular septa run into the lung and in them or nearby there are enormous lymphatics distended with a disintegrated fibrinopurulent material loaded with streptococci.

The bronchial walls are not really much altered in this lung. Some of them are slightly thickened and contain leucocytes and debris. There is a little infiltration of the alveolar walls about blood vessels and bronchi and there are areas of collapse with hemorrhage and desquamation of epithelium. But the most striking feature is the colossal distension of the lymphatics and it is around them that the infiltration and thickening of the alveolar walls are greatest.

Cultures from the lung showed *Streptococcus hæmolyticus* in both cases.

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Case 55.—O. F. D., age 22 yrs. Had measles at age of 7. On Dec. 27, 1917, developed measles and was in the hospital for 2 weeks. Went on duty Jan. 9, 1918, but was very weak. On Jan. 11 was brought to the hospital again with a stitch in his left side and dyspnea. After 9 days was able to walk about, but on Feb. 8 had a chill with severe pain in his left side, vomiting, and cough. Dulness over entire left side with flatness behind and below the middle of the scapula. Tubular breathing at the left apex becoming distant and suppressed at the base. Jaundice and cyanosis. Aspiration of thorax on Feb. 15, but no fluid was obtained. Flatness over whole left side with distant tubular breathing. On right side resonance somewhat impaired behind but good anteriorly; breath sounds bronchovesicular with few râles. On Feb. 16, 640 cc. of slightly turbid straw-colored fluid were withdrawn from the left chest and the patient was sent for operation which was performed on Feb. 18 with resection of a rib. Temperature became normal and drainage was good, but from about Feb. 26 to Mar. 7 when the patient died the drainage had decreased, there were signs of septic poisoning, and the temperature was irregular. Cultures from the circulating blood on Feb. 11 and 15 were negative. The sputum contained *Streptococcus hæmolyticus* and *B. influenzæ*. Fluid aspirated from the chest on Feb. 11 and 16 showed *Streptococcus hæmolyticus* alone. Autopsy Mar. 7, 1918.

Anatomical Diagnosis: Clinical history of measles. Lobular pneumonia with multiple abscess formation. Empyema (left). Seropurulent pleuritis (right). Infected infarcts of spleen.

Left pleural cavity.—In the line of the scapula on the left side there is a wound 12 cm. long running obliquely along the course of the rib from which a portion has been removed. The cavity is obliterated along the anterior margin of the lung and over its lower portion by old adhesions. The upper part of the pleural cavity is lined by thick yellowish fibrinopurulent exudate. Practically all the fluid exudate has escaped, but there is a pocket containing about 100 cc. of thick greenish pus between the diaphragm, the lower mesial surface of the lung, and the pericardium. This communicates with a space between the two lobes. *Right pleural cavity.*—Contains about 5 cc. of creamy purulent fluid which is spread over the back of the lung and to a less extent anteriorly where the pleura is still shining. The costal and diaphragmatic pleuræ are injected and have lost their gloss in the posterior part of the thorax. *Left lung (Fig. 42).*—The upper lobe is firm except in its anterior lower part which is collapsed. On section it is found that the whole posterior part from the apex down is dense, greyish yellow and moist, but rather thickly studded with patches of opaque pale greenish yellow. At the apex there is one such mass about 2 cm. in diameter and in the lower part there is a great group of them reaching up to the pleura and only partly separated from each other. These patches have softened and partly liquefied foul smelling central portions and hemorrhagic margins. The more anterior part of the lobe shows thickened interlobular septa and numerous smaller nodular consolidations. The lower lobe is

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more flabby and of darker reddish grey color. The interlobular septa are also rather conspicuous and in the lobules there are to be found numerous projecting nodules. There are also several large yellow abscess-like masses. The bronchial glands are large, soft, and grey. *Right lung.*—The lung is very voluminous (Fig. 43) and the upper lobe easily inflated with air. On section the upper and middle lobes and the anterior portion of the lower lobe are air-containing. The posterior portion of the lower lobe is dark purplish, airless, and fairly firm. There project from its surface a number of opaque firm yellow areas some of which are 3 cm. in diameter. They are partly hidden by the reddened pleura, but in places show through as opaque yellow patches. A similar mass projects from the posterior part of the middle lobe. On section the lower lobe is collapsed and studded throughout, even in the air-containing part, with yellow opaque nodules, the smaller of which seem to have a central lumen. The large ones are quite like those in the upper lobe. *Spleen.*—Measures 19 by 11 by 5.5 cm. It is quite firm, especially in certain greyish projecting portions which are irregular in outline and surrounded by a red border. On section much of the spleen is greyish in color with distinctly visible trabeculæ and Malpighian bodies. The splenic pulp is swollen, shining, and velvety. In contrast to this there are irregular patches with ragged outline extending deep into the substance of the organ and bordered by a broad margin of hemorrhage. These patches are dry and opaque with a dull greyish red color.

Cultures from the heart's blood showed *Streptococcus hæmolyticus*, and similar Gram-positive cocci were found in abundance in films from the spleen and pericardial and pleural fluids, but all autopsy material was grossly contaminated with a Gram-negative spreading bacillus with putrefactive odor.

Microscopic Examination.—The greatly thickened pleura over the left lung is dense and fibrous and covered with fibrin. The interlobular septa are not especially conspicuous on section. The bronchi although filled with purulent exudate are scarcely thickened or infiltrated. The exudate contains streptococci and Gram-negative bacilli which appear to be influenza bacilli. The alveolar walls are nowhere especially thickened nor do they show any extensive desquamation of epithelium. The alveoli are filled with fluid and leucocytes. There are certain areas in each section which show the especial filling of the alveoli with leucocytes and in these there are whole patches of the central alveoli in which walls and exudate are completely necrotic. In these alveoli streptococci are extraordinarily abundant. They are present in short chains, in tangled masses, or engulfed singly by leucocytes.

Throughout both lungs the changes appear to be the same. They are definitely areas of lobular pneumonia with large numbers of streptococci causing necrosis and liquefaction, and surrounded by an edematous lung tissue in which the changes characteristic of the interstitial bronchopneumonia do not appear. But there are some areas especially near the thickened pleura where the interlobular septa are wider and infiltrated, and the bronchi and blood vessels and

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even the alveolar walls share in this infiltration. The alveoli in these areas are mostly collapsed, but some are distended with leucocytes and great quantities of streptococci. Most striking is the fact that the lymphatics are enormously distended in many places and filled with a disintegrated mass of cells and bacteria. It is evidently from these that some of the large necroses begin, although in the collapsed lung around them there are numerous foci in which whole colonies of bacteria are surrounded by necrotic tissue.

The spleen shows irregular areas of necrosis edged with hemorrhage and studded throughout with veritable colonies of streptococci. The artery supplying one such area is plugged with a softened thrombus which contains the same great masses of organisms. The other organs show no such gross evidence of infection, although there is cloudy swelling of the liver and kidneys.

Case 56.—F. E., age 40 yrs. Had scarlet fever and measles in early life. For 6 weeks before entrance to hospital had pain in right side whenever he caught cold. On Feb. 7, 1918, had a chill, pain in side, and a temperature of 102° F. Entered the hospital Feb. 8, 1918. There was found dulness over the right lower lobe with distant bronchial breathing. Breathing over left side accentuated. Tenderness over abdomen with rigidity of muscles. Temperature 98° F. Leucocytes 24,400. On Feb. 26 the right chest was aspirated and the pleural fluid contained *Streptococcus hæmolyticus*. Temperature from 100–103° F. for the first 10 days. On Feb. 19 it fell abruptly to normal and later fluctuated from 98 to 101° until Feb. 26. Respiration 40, pulse 100–128. On Feb. 26 the 7th rib was resected under local anesthesia and the right pleural cavity drained. Died Mar. 7, 1918. Autopsy Mar. 8, 1918, 10 a.m.

Anatomical Diagnosis: Confluent lobular pneumonia with empyema and extension through diaphragm. Pericarditis with effusion. Axillary cellulitis.

Left pleural cavity.—Free from adhesions. Contains a small amount of fluid, but the surfaces are smooth and glistening although slightly hyperemic posteriorly. *Right pleural cavity.*—Partly obliterated by very dense fibrous adhesions which enclose a pocket filled with greenish yellow purulent fluid. There is an incision over the 8th rib in the right lateral scapular line which allows the escape of pleural fluid through a rubber drainage tube. The tissue about this wound is very edematous and the margins are necrotic. *Pericardium.*—Contains 100 cc. of yellow purulent fluid with floating shreds of fibrin. The surfaces are covered with a thick fibrinopurulent exudate. Endocardium normal. *Left lung.*—Surface is smooth and lung is normally air-containing throughout. *Right lung.*—The pleura is 3 mm. thick and very dense. It is covered with a layer of fibrin in places. The upper lobe is air-containing. The lower lobe is dense and uniformly grey and consolidated with a few scattered flecks of more hemorrhagic appearance. There is no thickening of the septa or walls of the bronchi.

Microscopic Examination.—The left lung is normal. The right is in part edematous with a scattered exudate of polymorphonuclears. The lower lobe, however, shows a compact exudate of these leucocytes filling the alveoli. Septa,

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bronchial walls, and alveolar walls are delicate and not infiltrated with mononuclear cells.

No cultures were recorded.

The right lung at its base is adherent to the diaphragm and between them there is a collection of fibrinopurulent exudate. This is seen to extend through the diaphragm so that the dome of the liver is also covered with a localized fibrinopurulent exudate.

Case 187.—E. S., age 23 yrs. Had German measles on May 2, 1918. On May 6 moist râles throughout both chests, with bronchial breathing in right upper lobe. On May 12 dulness over left upper lobe with fine crepitant râles and high pitched expiration. Friction rub in right axilla. Bronchopneumonia of both lungs on May 8. Sputum on May 8 was purulent, homogeneous, slightly blood-tinged, with a few Gram-positive diplococci. Cultures show predominant staphylococcus, few colonies of hemolytic streptococcus. Blood culture was negative May 7, 1918. Died May 13, 1918, at 8.40 p.m. Autopsy May 14, 1918, 14 hours after death.

Anatomical Diagnosis: Confluent lobular pneumonia (both upper lobes). Disseminated lobular pneumonia with slight interstitial changes. Rupture of rectus abdominis muscle.

The sheath of the rectus abdominis muscle bulges into the peritoneal cavity on each side at a point just below the umbilicus. On incision it is found that the muscles are torn across and that the ends are retracted leaving a space filled with blood clot and bloody fluid. This rupture is symmetrically placed on the two sides. The ruptured muscle is contracted into a thick belly on each side and there are opaque greyish yellow discolorations seen in the substance of the broken ends. The peritoneal cavity contains no excess of fluid and the surfaces are smooth and glistening. *Left pleural cavity.*—The cavity is partly obliterated above by old fibrous adhesions and there are similar adhesions between the base of the lung and the diaphragm. The free portion of the pleural cavity contains about 20 cc. of clear fluid and the surfaces are smooth. *Right pleural cavity.*—Contains very little fluid. The surfaces are smooth except over the upper lobe where there is a thin fibrinous exudate. *Left lung (Fig. 44).*—The lung is voluminous and in part covered with shreds of old adhesions. The upper lobe is air-containing anteriorly, but firm posteriorly. On section there is found a large area of complete consolidation which is pinkish grey in color and fairly smooth although plugs of exudate can be seen projecting from the alveoli. The bronchi in this area are wide with a dull grey lining, and contain a grey purulent exudate. Scattered through the area of consolidation there are irregular patches which are still more prominent and of a lighter yellowish color and more opaque than the rest. These are softened and even partly liquefied in places. In the anterior air-containing portion there are some nodular consolidations about the branches of the bronchi. The lower lobe is in general air-containing but is rather firm posteriorly. Throughout it there are scattered

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small peribronchial consolidations such as are seen in the anterior part of the upper lobe. These are more numerous and larger in the posterior part of the lobe. They are not accompanied by any marked hemorrhage. The bronchial glands are much enlarged and are dark greyish red. *Right lung.*—The lung is large and in general seems to be air-containing. It is found, however, that there is in the posterior middle portion of the upper lobe an area of consolidation about 4 cm. in diameter which on section is greyish pink and smooth. Part of the area is yellowish and opaque and appears to be beginning to soften. The anterior part of the lobe is air-containing. The middle lobe is air-containing except for some of the bronchioles which are thickened and filled with exudate and in places surrounded by nodular areas of consolidation. In the lower lobe of this lung there are many bronchioles whose lining epithelium is entirely lost and the surface of the exposed tissue necrotic. These bronchi have greatly thickened walls with extreme hyperemia and infiltration with mononuclear cells. The adjacent alveoli are generally collapsed, their walls infiltrated with mononuclear cells, and their cavities with blood, fluid, and epithelial cells. *Pharynx and larynx.*—The tonsils are not enlarged. The pharynx is rather pale. The larynx is only slightly reddened and there are no ulcers on the vocal cords or epiglottis. The trachea is slightly reddened. The cervical lymph glands are edematous and greyish red.

Cultures at autopsy showed *Streptococcus hæmolyticus* in the heart's blood, right and left lungs, and in the bloody fluid between the torn ends of the rectus abdominis muscles. Smears from these localities showed these organisms alone.

Microscopic Examination.—The lung shows remarkable changes. The pleura is perhaps somewhat thickened over the left lung, but there is no exudate or granulation tissue formation. The interlobular septa are wide and edematous, and contain wide lymphatics which are not thrombosed or at most contain a strand of fibrin. They contain abundant streptococci. The area of consolidation in the upper lobe shows no bronchi conspicuous for their thickening, although there is a definite mononuclear infiltration of the walls in some cases. The alveolar walls are not infiltrated or thickened. The alveoli are densely packed with polymorphonuclear leucocytes with little fibrin and scarcely any blood (Fig. 45). These leucocytes are fairly loaded with micrococci and there are great quantities of these organisms free between them. It appears as though the leucocytes were inadequate to engulf all of them.

The alveolar walls are noticeably pale and flattened or thinned out in places. With Weigert's fibrin stain it suddenly becomes evident that the capillaries in many of the alveolar walls are completely obstructed by fibrinous coagula which are not quite homogeneous but fill the whole network of capillaries, at times in such a way as to demonstrate this network as though by a purple injection mass (Fig. 46). Evidently the obstruction to circulation is great and such areas are widely necrotic, there being no nuclei of the alveolar wall left intact enough to stain. Doubtless these are the opaque yellowish patches observed in

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the consolidated area in the gross inspection. This consolidation is very dense and extends over a large area in the manner of a lobar or confluent lobular pneumonia.

In the portion of the lung which is not the seat of a uniform consolidation the bronchi are more definitely thickened by the great hyperemia and new tissue formation which is so often seen. But there is no characteristic surrounding zone of thickening of the alveolar walls with desquamation of the epithelial cells, hemorrhagic organization of the exudate, etc. Instead there are minute patches of lobular consolidation in every respect resembling the large patch in the upper lobe. In the outlying area where there is a great deal of edema this fluid is loaded with bacteria. In places it contains numerous vacuoles which vary greatly in size but are peculiarly surrounded by bacteria which appear to float on the surface of the vacuole. These cavities may be air bubbles from the mixing movement of the fluid and the bacteria may swim on their surface in order to be in contact with air, or else their position may be merely an effect of the surface tension of the fluid. The same phenomenon was observed with pneumococci in Case 31.

There is, therefore, an extraordinarily intense infection with *Streptococcus hæmolyticus* which produces a confluent lobular pneumonia resembling a lobar pneumonia in places, with only traces of its usual interstitial action. The right lung is similar. Careful search failed to reveal any influenza bacilli.

Microscopically the rectus muscle shows extensive reduction of muscle fibers to hyaline formless clumps. Where the rupture has occurred there is, of course, much hemorrhage and the separation of fragments of completely necrotic muscle tissue which had already shown the hyaline change in the substance of each fiber. Streptococci are present in quantities in the necrotic ends. The hyaline clumps are found within the sarcolemma sheaths quite far back. They are invaded by wandering phagocytic mononuclear cells which can be distinguished from the shoals of sarcolemma nuclei by their more chromatin-rich nucleus. The sarcolemma nuclei are pale with one deeply stained nucleolus.

Case 192.—J. R. B., age 23 yrs. No history of measles or other predisposing disease. Began suddenly on May 5, 1918, with a chill and pain in the chest. The diagnosis of lobar pneumonia involving the left lower lobe was made on May 11. Blood culture on May 14 was negative, but the sputum contained *Staphylococcus aureus* and influenza bacilli. Died May 14, 1918. Autopsy May 15, 1918, 15 hours after death.

Anatomical Diagnosis: Hemorrhagic bronchopneumonia (bilateral). Ulcerative laryngitis.

Left pleural cavity.—Contains only about 5 cc. of clear fluid. The pleural surfaces are smooth but flecked with hemorrhage posteriorly. *Right pleural cavity.*—The cavity contains a little clear fluid. There are a few easily torn adhesions over the apex of the lung. The pleural surfaces are smooth but the lower lobe of the lung is deep blue and covered with areas of hemorrhage.

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Left lung (*Fig. 47*).—The upper lobe is found to be air-containing throughout, with the exception of very minute foci about the terminal bronchioles which stand out as greyish opaque points. The lower lobe receives a little air in the anterior part. The remainder is deep red and rather nodular looking although the nodules do not stand out very distinctly. They appear rather as greyish centers of reddened hemorrhagic areas. *Right lung* (*Fig. 48*).—The lung is much more voluminous than the left. The upper lobe is firm in its apical portion but otherwise air-containing. The firmness is due to the presence of scarred and pigmented areas at the apex and a little lower on the posterior side. In the lower portion of the lobe posteriorly there are several branching nodular consolidations which surround the ends of the bronchi. The middle and lower lobes contain a little air anteriorly but are consolidated posteriorly, the consolidation being produced by greyish nodules surrounded by deep red confluent hemorrhages. The bronchial lymph nodes are large and greyish red. *Pharynx and larynx.*—The pharynx and base of the tongue are deeply reddened and the lateral walls of the pharynx are covered with an opaque yellow mucoid layer. There is similar congestion of the larynx and trachea, but this does not extend into the esophagus. There are slight erosions of the edges of the epiglottis and a shallow ulceration in the wall of the larynx at the attachment of the vocal cords, but the cords themselves are not ulcerated.

Cultures at autopsy gave *Streptococcus hæmolyticus* from the heart's blood and lungs.

Microscopic Examination.—The lungs show a fairly uniform process on both sides which is different from any previously described.

The pleura is densely infiltrated with blood. All crevices and the lymphatics are distended with blood. The interlobular septa are not conspicuous, and where they are found they are in places edematous and infiltrated with mononuclear cells and blood. The lymphatics are not prominent but often contain blood and leucocytes. The bronchi are filled with polymorphonuclear leucocytes and blood cells. Their walls have usually lost their epithelium and are very hyperemic and edematous but not really thickened or infiltrated with cells. The adjacent alveoli are usually filled with leucocytes. Their walls are not thickened although in places there are leucocytes in their substance. Further from the bronchi the alveoli contain fewer leucocytes and are more and more filled with blood. Indeed, except for the peribronchial filling of the alveoli with leucocytes the whole lung is nearly solidly filled with red corpuscles with which a few desquamated epithelial cells and leucocytes are mingled. The whole area is one vast hemorrhage. As a rule, few or no bacteria can be found but there are some patches in which streptococci are present in great numbers, sometimes scattered in single chains, sometimes in dense clumps or tangles of chains. Since influenza bacilli were found in the sputum and since the lesion in this lung is so totally unlike that seen in other cases of streptococcus pneumonia the idea suggests itself that it may be due to the influenza bacillus, and search in sections properly stained shows the presence of enormous numbers of minute Gram-

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negative organisms which may be influenza bacilli, although they often occur in short chains.

Section of the rectus abdominis (Fig. 49) shows the most extensive hyaline degeneration of the muscle fibers which are reduced to formless clumps of red-staining material still enclosed in the sarcolemma sheath. There are still some intact fibers among the altered ones. The nuclei of the sarcolemma sheaths show no alteration and there is no inflammatory reaction.

Case 195.—G. M., age 23 yrs. Negro. Began with measles on May 3, 1918, and developed pneumonia which was thought to be a lobar consolidation of the right lower lobe on May 10, 1918. Died May 16. Autopsy May 17, 1918, 11 hours after death.

Anatomical Diagnosis: Clinical history of measles. Disseminated lobular pneumonia. Empyema (left).

Left pleural cavity.—Contains 450 cc. of yellowish fluid with flakes of fibrin. The surfaces are covered with a yellowish fibrinous exudate but there are no adhesions. *Right pleural cavity.*—Contains about 50 cc. of a slightly cloudy fluid. There are on the pleural surface numerous small discrete roughened brownish patches. *Left lung.*—The upper lobe is air-containing throughout. In the lower lobe there are numerous nodular masses of consolidated tissue which measure 2 by 6 mm. in diameter and surround the bronchioles. These become more numerous in the posterior part of the lobe and are often confluent. *Right lung.*—There are nodular consolidations scattered throughout all the lobes, becoming more numerous and close set as one passes towards the posterior part of the lung. In the upper lobe they are fairly discrete but occupy a large proportion of the lung substance posteriorly. In the middle lobe there is also a larger area of consolidation, a patch 2 cm. in diameter which is firm and grey at the periphery but rather more rose-colored in the center. In the lower lobe the nodules are very numerous especially in the posterior part. The mucosa of the bronchi and trachea is hemorrhagic and deep red.

No cultures were made at autopsy.

Microscopic Examination.—The pleura is found to be hyperemic and slightly thickened but still covered by its lining layer of cells. There is a thick layer of fibrin overlying it but there is no sign of organization. The interlobular septa are everywhere wide and edematous. The lymphatics are also wide, and while some of them may be traced along in the septa filled with fluid only, most of them are distended with a compact mass of disintegrated leucocytes, blood, and fibrin with bacteria. Everywhere in the walls of bronchi and blood vessels, in the interlobular septa, and in the pleura the lymphatics are very wide and conspicuous.

The lung in general is edematous, the alveoli are filled with what appears to be a rather viscid fluid. There are focal areas of consolidation which were recognized in the gross and can be seen as such by the unaided eye in the stained section. It is difficult to outline these as they shade off into the adjacent tissue in which there is only edema with desquamated epithelial cells. But it is clear that

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there are numerous patches of completely consolidated lung tissue in which every alveolus is filled with polymorphonuclear leucocytes. In and especially about these there is much hemorrhage and then further out the alveoli are found to contain only fibrin with fluid and mononuclear cells which are probably desquamated epithelium. The bronchi are not at all conspicuous. They contain leucocytes and bacteria. The walls are hyperemic but not infiltrated with cells, nor are the alveolar walls thickened or infiltrated at any point. The most prominent feature in these areas is constituted by the great thrombosed lymphatics. In places and perhaps especially in these lymphatics the leucocytes are necrotic and disintegrated. In the middle lobe of the right lung the area of uniform infiltration with polymorphonuclears is much greater. There are hyaline thrombi in the capillaries of the alveolar wall and much necrosis of the exudate and of the walls. The bronchi are but little altered. The consolidation even here is patchy with alternation in the types of exudate.

In these cases the pleural effusion is quite like that in the preceding groups and it is somewhat surprising to find that a man may survive for 55 days with this lesion extensively developed in association with an old empyema. The gross appearance of the lungs is usually different from that found in interstitial bronchopneumonia, since these areas of consolidation are no longer nodular, hard, and prominent, nor especially situated about the branches of the bronchi. Instead, they are very rough, grey, and slightly elevated, often confluent in quite large patches where they resemble closely in their texture the consolidation of pneumococcal lobar pneumonia. But in many cases they are intensely hemorrhagic and in the central parts dull and opaque. As an example of the first type Case 187 may serve, in which a large area of homogeneous consolidation with granular exudate projecting from the alveoli occupies part of the upper lobe, while smaller areas of the same sort are scattered through the lower lobe. In Cases 20 and 192 the areas of consolidation are large and hemorrhagic.

In all these the participation of the lymphatics is extremely striking. Great beaded canals distended with opaque yellow pus so as to become very conspicuous accompany the blood vessels and bronchi or run in the line of the interlobular septa to the pleural surface. These stand out especially in Cases 20 and 26 and can be readily traced to their connection with the network in the pleura which is similarly prominent and distended with pus.

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In Case 55 extensive areas of necrosis occur in which the lung substance is converted into a soft yellow opaque material. These areas look like abscesses as they project under the pleura and possibly they should be so called, but they are really pretty firm opaque necrotic patches of consolidated lung swarming with streptococci but still composed of coagulated tissue and not of pus. There is no real distinction except perhaps in the lack of an intense leucocytic invasion to reduce this necrotic material quickly to a liquid state. In other cases it has been seen that such areas may be discharged through a bronchus the walls of which are interrupted on entrance into the necrotic patch. This leaves a cavity which may or may not communicate with the pleural cavity. In none of our cases had this actually occurred, but it seems that this is the explanation of the formation of the pleurobronchial fistulæ which are encountered by many surgeons in treating the late empyema cases.

Microscopically the lesions just mentioned are the outcome of the filling of alveoli with streptococci and an exudate of leucocytes and fibrin. The streptococci are extremely abundant throughout this exudate. In Case 187 in which the consolidation is almost lobar in appearance the capillaries of the alveolar walls are widely thrombosed with hyaline strands of fibrin which completely occlude them. The exudate and even the tissue of the lung becomes necrotic under these conditions.

In the more hemorrhagic consolidation such as is seen in Case 20, great stretches of lung substance simply become necrotic and filled with blood without any adequate infiltration of leucocytes. In such places the streptococci in long chains form a tangled matted growth as though they were growing in the most favorable culture medium. In the outlying parts of the lung about these places there are alveoli filled with leucocytes and fibrin but the destructive process seems to have been too intense and rapid to allow the institution of a proper reaction. The lymphatics distended with leucocytes, fibrin, and myriads of streptococci form enormous objects in the microscopic field.

The lesion then in all these cases is produced by the streptococcus; it is the simplest inflammatory reaction to the invasion of great numbers of streptococci and often even this reaction fails, so that with

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great extravasation of blood the whole invaded area becomes necrotic and a good soil for unlimited multiplication of the organisms. It represents the most passive attitude of the body in which resistance is at its lowest.

The Changes in Other Parts of the Respiratory Tract in Streptococcal Pneumonia.

No distinction is practicable between the groups of cases just considered in so far as the lesions of the rest of the respiratory tract are concerned. The changes in the lung proper have been described and the forms of pleurisy will be analyzed later. There remain the bronchial glands, the larger bronchi and trachea, the larynx, and the upper air passages.

The bronchial lymph glands are always somewhat enlarged although not so greatly as in some other affections of the lungs. They are soft, edematous, and greyish red except when deeply pigmented. I have encountered no abscesses in these glands. The cervical and peritracheal glands are often similarly affected. Microscopically they show in each case a considerable increase in the cells of the lymph cords and islands, but it is in the sinuses that the change is most marked. These are very wide and are packed with cells, chiefly large and small mononuclear wandering cells which have probably been swept into these sinuses from the lymphatics of the lungs since they are of the type seen there. They are to some extent phagocytic, loading themselves with the debris of other cells. There is no evidence that they are derived from the endothelium of the sinuses which is intact. Among these there are quantities of streptococci often single or in pairs, often in tangled masses.

The large bronchi and trachea are deeply reddened, covered with purulent exudate, and occasionally with a pseudomembrane which is generally limited to the bronchi. Streptococci are found abundantly strewn along the surface of the mucosa.

In the acuter cases and especially in those in which the disease is associated with measles there is aphonia with corresponding changes in the larynx. These changes, which are found in Cases 165, 178, 184, 192, 194, 180, and others, consist in an intense reddening of

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the mucosa often with some edema. Most striking, however, is the ulceration which commonly affects the vocal cords and causes a deep loss of substance along their whole edges. Microscopically it is found that the epithelium and underlying elastic tissue is necrotic or has been swept away completely leaving the base of the ulcer thickly strewn with streptococci. Streptococci are found in crevices of the neighboring tissue and in folds of the mucosa nearby. Similar ulcerations occur on the epiglottis, on the arytenoepiglottic folds, in the pyriform sinuses, and elsewhere, in the walls of the pharynx and larynx. In Case 165 there was a marked swelling of the arytenoepiglottic folds and of the epiglottis with only a shallow superficial ulceration, but all the swollen tissue was packed with streptococci and a diffuse inflammatory exudate. Most of the other cases, however, showed no especial alteration in the larynx. The walls of the pharynx are generally deeply congested and in a few instances there was a superficial ulceration of the uvula and of the pillars of the fauces. The tonsils are not much enlarged or altered in appearance, and although streptococci can be found in clumps in the depths of the crypts there is no especial reaction of an inflammatory character about them. We were, of course, concerned with the idea that the tonsils might harbor the streptococci and in this way play an important part in the development of the disease, but it is not even certain that the clumps of streptococci which often have a radial marginal arrangement are of the same character as those which produce the pneumonia. At any rate the impression received was that the tonsils are passive in this process. The hemolytic streptococcus from outside seems to sweep past them through the pharynx, the larynx, and trachea into the bronchi. At most they fail in their function as guards, and this may be said too of the lingual and other adenoid tissue which becomes slightly swollen.

The condition of infection of the accessory sinuses which communicate with the nasal cavity and of the nasal mucosa itself is unknown to me as there was no opportunity to investigate them. It seems, however, that they may be the first to become infected and they should be studied. It is evident that inflammation follows the extension of infection up the Eustachian tube to the middle ear, for otitis media is by no means uncommon as a complication (Cases 205, 21, 181).

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Lesions in Other Organs.

The channel of infection of the pericardium is not clearly decided. It seems probable that infection must take place by extension from the pleura although this is difficult to demonstrate, and it is puzzling to find so many cases of intense pleural infection without pericarditis.

In the whole series of 60 cases there were ten in which there was a definite pericarditis. Of these, two, Nos. 19 and 186, were associated with lobar pneumonia caused by the pneumococcus; two others, Nos. 36 and 46, occurred in cases in which the pneumococcus and streptococcus were both present, and the remaining six were in cases of streptococcus infection, although three of these at least, Cases 56, 57, and 176, were associated with very old empyema in which the bacterial flora was no longer uncontaminated. There are no sharply distinctive features in the streptococcus pericarditis, although there seems to be a tendency to great thickening of the pericardial tissues and the formation of obliterating adhesions. In one, Case 203, the pericardial sac was enormously enlarged and thickened and contained at autopsy 1,000 cc. of thick pus, although it had been aspirated by the surgeon some days before. The others presented a thick turbid purulent fluid with shaggy fibrinous exudate on the pericardial surfaces. There were several other cases in which minute hemorrhages and a slightly cloudy and somewhat increased fluid attracted attention to the pericardium, but in these the pericardial surfaces were still glossy.

Endocarditis was present in one case, No. 45, of lobar pneumonia, and the pneumococcus was isolated from the vegetations. One case, No. 24, showed a lobular pneumonia with some of the features of an interstitial bronchopneumonia in which there was acute endocarditis, but the body was partly decomposed, and although streptococci were present in smears the exact nature of the case is not clear. In none of the more definite instances of streptococcal pneumonia was there endocarditis.

The spleen in the cases of streptococcal pneumonia was sometimes slightly enlarged and occasionally rather soft. On the whole, however, it showed no definite change from normal, and microscopic examination failed to reveal any marked alteration of any part of its

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structure. In one case only, No. 55, which was a case of lobular pneumonia with large areas of necrosis or abscess formation and an empyema of 55 days standing, were there infarct-like infected areas scattered through the substance. These on microscopic examination showed the presence of whole colonies of streptococci and Gram-negative bacilli lying in the middle of necrotic and disintegrated areas.

The liver in most instances showed a moderate cloudy swelling, but otherwise no departure from the normal. In one case only, No. 16, were there fresh midzonal necroses throughout the organ.

In general the kidneys were normal in appearance except for a slight cloudiness of the cortex which appeared in microscopic section as a slight swelling of the epithelial cells of the convoluted tubules. But in four cases, Nos. 35, 36, 171, and 188, there was an acute nephritis with petechial hemorrhages and swelling and some opacity of the cortex. Microscopically these cases showed glomerular lesions characterized by hyaline thrombosis of the capillaries with hemorrhage and exudation of leucocytes into the Bowman's capsules and tubules and the accumulation of leucocytes and wandering cells in the interstices of the tissue. Epithelial degeneration was present in only moderate degree. But of these four cases two, Nos. 36 and 188, were essentially pneumococcus infections and were really cases of lobar pneumonia. Acute nephritis therefore occurred in only two of the cases of streptococcal infection and cannot be regarded as a characteristic accompaniment of this infection but rather as an accidental occurrence.

The peritoneal cavity was infected, however, in several cases, so that acute peritonitis seemed to be a not infrequent accompaniment of the streptococcal pneumonia.

In this series five cases in all showed an acute peritonitis and of these one, No. 51, was a case of pneumococcal pneumonia with pneumococci in the peritoneal exudate. In the others, Nos. 35, 165, 176, and 194, the peritoneal exudate contained the streptococci. They were all rather old cases of streptococcal pneumonia with empyema. No origin could be found for the peritoneal infection in the abdominal organs, and it may be that extension of the infection occurred through the lymphatics of the diaphragm. Indeed it seemed possible to trace this directly in Case 194.

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In Case 56 there was a gross extension of the infection through the diaphragm so that an abscess-like accumulation of pus on the pleural surface communicated freely with a similar enclosed pocket on the upper surface of the liver.

The testes show in nearly all these cases an extraordinary change which is especially striking in the streptococcal infections, although occurring sometimes in the pneumococcal infection and failing to appear in some of the streptococcal ones. It appears to consist in a cessation of spermatogenesis which has probably come about through a stoppage of mitosis at an early stage. In most of the cases of streptococcal infection spermatozoa are not to be found in the tubules of the testis, although a few may persist in the seminal vesicles embedded in the viscous fluid which is found there. Not only are the spermatozoa absent, but in many cases one looks in vain for spermatids or spermatocytes. The spermatogonia are always present, and the Sertoli cells become very conspicuous, but with only these types of cells left the tubule is reduced to an extremely simple structure.

The interstitial tissue is less altered although frequently greatly increased in bulk. Leydig's cells are generally unchanged. It is possible that older changes, such as the complete conversion of the tubules into hyaline strands, and even the great thickening of the interstitial tissue may be the remains of some earlier injury such as may have resulted from mumps. But the cessation of spermatogenesis is so constant that it must be ascribed to the present disease. Among the cases of pneumonia caused by the pneumococcus two or three showed normal tubules, but the rest exhibited various stages in the same process leading to the interruption of formation of spermatozoa.

This matter has been discussed by Cordes, who found this condition after many acute infections. Details of the present material need not be given here.

Bone marrow taken from the femur in a great number of these cases showed uniformly an increase in the cell content, depending especially upon an increase in the myelocytes. It was not different from that observed in many other acute infections accompanied by leucocytosis.

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In Cases 187 and 205 there was found a symmetrical rupture of the two sides of the rectus abdominis in its lower third. The separation of these torn ends was accompanied by the production of a considerable hematoma such as is often seen in the same position in typhoid fever—the so called Zenker's degeneration of the muscle. Study of these and other rectus abdominis muscles shows that there is a most extensive hyaline degeneration of the fibers which are broken into irregular masses of glassy material with no trace of the former striations. These become surrounded by the concentrated nuclei of the sarcolemma sheath and new cellular connective tissue springs up between them. Before long such weakened muscles tear with coughing or some other strain and the hemorrhage occurs. In Case 187 the streptococcus was found in the bloody fluid, but in the other there were no bacteria. In Case 192 there was no such rupture, but although the rectus muscle looked normal it showed microscopically a very extensive degeneration of its fibers (Fig. 49). Muscle taken from the corresponding point in several other cases failed, however, to show any degeneration. It seems probable that this is not the direct effect of infection, but that it is caused by some toxic process after which bacteria may lodge on the necrotic material.

In another case, No. 45, in which the pneumococcus was found in the pneumonic lesion there were symmetrically placed abscesses in the same position occupying most of the substance of the lower third of the rectus abdominis on each side. In these the pneumococcus was found. Several other cases of this kind were observed at Fort Worth, Texas.

The lodgement of streptococci in other parts of the body, such as the bones, joints, and muscles, appears not to be very common.

In Case 176 in which there was an old empyema there was found an extensive abscess among the muscles of the neck reaching upward toward the left ear and downward past the dome of the pleura into the muscles between the scapula and the vertebral column. How the infection reached this region is not clear. The pleural cavity was not in communication with the abscess, and the shoulder joint was normal although surrounded. It seemed possible that it might have been due to extension from the pleura, but this was not proven. In no other case was there any such area of infection away from the res-

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piratory organs themselves. Nevertheless I have heard from various surgeons of the occurrence of abscesses in the muscles and subcutaneous tissues in different localities. Although joint infections have been described we met with none in these cases.

The question of the existence of a streptococcal septicemia is much discussed and there are differences of opinion on the point. We have made in all about 100 blood cultures[5] from the circulating blood taken from the arm vein at various times before death with the usual technique of adding the blood to sterile broth, etc., but none of these cultures gave a positive result except when they were taken just before death. Even then there were very few positive results and the contrast between this organism and the pneumococcus is made more striking by the fact that in the cases in which lobar pneumonia is found combined with interstitial bronchopneumonia the pneumococcus has been isolated from the circulating blood, but not the streptococcus. Of course after death the heart's blood gives invariably a culture of the streptococcus. It seems that the conditions produced by the streptococcus are once more comparable with those produced by the tubercle bacillus, because in chronic phthisis we do not find the tubercle bacilli circulating in the blood as must be the case in generalized miliary tuberculosis; nevertheless scattered tubercles in all the organs attest the fact that at least a few tubercle bacilli are able to enter the blood stream. So with the hemolytic streptococcus. Its distribution is chiefly local in the respiratory tract, but enough streptococci may from time to time enter the blood stream to give rise to an occasional abscess.

4. Lobar Pneumonia.

Case 18.—J. P. W., age 30 yrs. Previous history negative. Developed cold and hoarseness Jan. 14, 1918. Entered hospital Jan. 26, with nausea and vomiting, chill, fever, and cough. Pain in back and right shoulder. Dulness, prolonged expiration, increased vocal fremitus, and crepitant râles over lower left back. Leucocytes 19,000. Temperature 104–101° F., pulse 100–150, respiration 26–50. Developed signs of consolidation at right base Feb. 1 and died Feb. 3. Autopsy Feb. 3.

[5] These cultures were made by the Commission in Texas, and at Camp Dodge by Captain Sellards and Lieutenant Toomey.

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Anatomical Diagnosis: Lobar pneumonia (left lung) with fibrinous pleuritis.

Left pleural cavity.—Obliterated by fresh fibrinous adhesions anteriorly, but in the posterior part there are 200 cc. of turbid fluid. The lung is covered with an edematous layer of fibrin measuring 2 cm. in thickness in places. *Right pleural cavity.*—Contains no fluid, surfaces glistening. *Left lung.*—The upper lobe is air-containing anteriorly, but in its posterior portion is completely and uniformly consolidated. In the anterior portion there is also a patchy consolidation with a few masses of yellowish fibrinous material embedded in the substance of the lung. In other places the walls of the vessels and bronchi are edematous. In the lower lobe the consolidation is uniform and of a greyish red color. It is distinctly produced by the filling of the alveoli with exudate. *Right lung.*—With the exception of the posterior portions of the upper and lower lobes which are atelectatic and a small area of consolidation in the upper lobe, the lung is air-containing. The bronchi are normal in appearance.

Microscopic Examination.—The left lung shows a loose thick layer of fibrin upon its surface. The pleura itself is slightly thickened by hyperemia, edema, infiltration of leucocytes, and some new formation of connective tissue cells. The layer of cells lining the pleural cavity is still visible, however, and no organization of the overlying fibrin has occurred. Numerous pneumococci can be seen scattered through the layer of fibrin and usually enclosed in phagocytic leucocytes. The same condition is found in the interlobular space where the surfaces are bound together by fibrin, but there organization appears to have begun.

The bronchi contain an exudate of leucocytes and red corpuscles. The alveoli are uniformly filled with an exudate of red corpuscles, leucocytes, and fibrin. Pneumococci are seen scattered diffusely in the exudate, both in the bronchi and alveoli. It is clear that the fibrin is more conspicuous in the alveoli adjoining the interlobular septa, but organisms are not obviously more abundant in the more central parts adjacent to the bronchi. The alveolar walls are distinctly infiltrated with leucocytes and occasional mononuclear cells. So too are the bronchial walls and walls of blood vessels, as well as the interlobular septa. This is not enough to make them prominent, however, and in general all these structures are but slightly thickened. The lymphatics in the bronchial walls, adventitia of blood vessels, interlobular septa, and pleura are greatly distended with a network of fibrin entangling red corpuscles and leucocytes. In these pneumococci are found. Some of these lymphatics are enormous and readily visible to the naked eye as yellow beaded strands in the consolidated lung.

The bronchial lymph glands are extremely hyperemic and the afferent lymph sinuses are greatly distended with red corpuscles and large phagocytic mononuclear cells. Pneumococci are abundant there, but there are few in the remainder of the gland.

Cultures showed Pneumococcus Type IV from the heart's blood and both lungs.

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Case 19.—B. N., age 27 yrs. Previous history negative. Taken sick suddenly Jan. 29, 1918, with vomiting and pain in the right hypochondrium. Entered hospital Jan. 30, and on Jan. 31 complained of acute pain in right chest. Dulness over upper lobe of right lung. Leucocytes 18,800. Temperature 101–103° F., falling to 99° before death. Pulse 90–130. Died Feb. 3. Autopsy Feb. 4.

Anatomical Diagnosis: Lobar pneumonia (right upper lobe) with fibrinopurulent pleurisy. Fibrinopurulent pericarditis with abundant effusion.

Left pleural cavity.—Contains a little brown fluid. Surfaces are covered over the lower lobe by a thin fibrinous exudate. The lung is adherent at the apex posteriorly. *Right pleural cavity.*—The anterior portion of the lung is glued to the parietal pleura and to the pericardial sac. Between the pericardium and the mesial surface of the lung there is an encapsulated cavity containing about 100 cc. of fibrinopurulent exudate. The posterior part of the pleural cavity is filled with similar exudate which bathes the lower lobe. Its surface is covered with a thick layer of fibrinous exudate. The upper lobe is adherent by fresh fibrinous adhesions to the costal pleura. *Left lung.*—Air-containing throughout. The bronchial glands are soft and pigmented but not enlarged. Bronchi are pale and contain sticky mucus. *Right lung.*—The upper lobe is uniformly consolidated, the cut surface showing a greyish red exudate which fills all the alveoli. The interlobular septa are prominent, the bronchi distended with opaque yellow exudate. The middle and lower lobes are almost entirely collapsed except in their anterior margins. There is no consolidation. *Pericardium.*—The pericardial sac contains 550 cc. of a thick greenish turbid fluid with floating shreds of fibrin. The surfaces are thickly covered with yellowish fibrinous exudate.

Microscopic Examination.—The consolidated part of the right lung shows a thin pleura with a covering of fibrin which is not organized; the lining cells of the pleura are still visible. The interlobular septa are widened and edematous, and a network of fibrin extends throughout their length. Numerous pneumococci are found scattered through the fibrinous exudate on the pleura and many are enclosed in phagocytes. The bronchi contain a purulent exudate. The walls are slightly thickened and infiltrated with mononuclear cells. The alveolar walls are in general thin but some are infiltrated with leucocytes, and in the neighborhood of the large vessels, broad interlobular septa, and pleura there is a thickening of the alveolar walls by mononuclear infiltration.

In the alveoli the exudate, composed of red corpuscles, leucocytes, and fibrin, is loaded with pneumococci which are uniformly scattered. Some of them are in phagocytes. Even the alveolar walls are occasionally invaded by them. The lymphatics are everywhere greatly distended with a clotted exudate of leucocytes and mononuclears together with large quantities of pneumococci.

There is a fresh pericarditis. The lining layer of cells is still complete and the fibrinous exudate is alternately compact and loose.

Cultures from the lung show Pneumococcus Type II.

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Case 25.—F. G. W., age 24 yrs. Previous history negative. Measles and mumps at 6 years. On Jan. 30, 1918, had a chill followed by fever and pain in right side. Entered hospital Feb. 1, expectorating rusty sputum. Dulness and tubular breathing over both sides posteriorly. Extreme cyanosis. Leucocytes 19,800. Temperature 99–103° F., pulse 110–140, respiration 25–35. Died Feb. 6. On account of the coarse bubbling râles it was suggested that the pneumonia was in the stage of resolution. Cultures from sputum and circulating blood gave Pneumococcus Type II. Autopsy Feb. 6.

Anatomical Diagnosis: Lobar pneumonia (bilateral). Fibrinous pleuritis.

Left pleural cavity.—Contains no excess of fluid. There are old adhesions over the posterior portion of the lung. *Right pleural cavity.*—Surfaces are glued together by fibrin and there is no fluid. *Left lung.*—The upper lobe is soft and cushiony and, although much pigmented, is air-containing throughout except for small areas of consolidation in the lowermost portion. The lower lobe shows extensive though somewhat patchy consolidation in which the individual alveoli are seen to contain plugs of exudate. *Right lung.*—The anterior part of the upper lobe is air-containing. The posterior part of the upper lobe, the whole of the middle lobe, and all of the lower lobe except the lowermost margin are consolidated. This consolidated tissue on section is smooth and grey and uniform in appearance; the alveoli are not easily made out to contain individual plugs.

Microscopic Examination.—The right lung shows an intraalveolar consolidation which stops sharply at the limit of the lobe. The interlobar cleft is filled with fibrin entangling a few leucocytes. The pleural cells are well preserved and on the pleural surface covered with a thin layer of fibrin which is not organized. The bronchi show no modification of their walls except a subepithelial accumulation of polymorphonuclear leucocytes. The lumen of each bronchus is filled with leucocytes. The alveolar walls are distinctly thickened (Fig. 50) through the accumulation of polymorphonuclear leucocytes between the capillaries and within the substance of the alveolar wall in such a way as to lift up from the capillaries into rounded eminences what seems to be a very thin structureless membrane upon which the alveolar epithelium lies. The thickening is thus very uneven and the alveolar surface of one of the walls presents a series of mammillations. In general the epithelial cells are greatly swollen and most of them are desquamated. The alveoli contain a loosely attached and rather shrunken network of fibrin with granular looking leucocytes and very numerous large round mononuclear cells which are active phagocytes and are stuffed with fragments of leucocytes. Pneumococci have been found by Weigert's stain in small numbers. There is much pigment in the lung, and interlobular septa as well as vessel and bronchial walls are loaded with it. Other portions of the lung where there is no consolidation are normal except for this.

Cultures from the lung showed Pneumococcus Type II.

Case 33.—D. K., age 21 yrs. Began about Jan. 5 with a cold and chilly feeling after exposure to rain. Entered hospital Jan. 9, 1918, with fever, headache,

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cough, and a macular eruption which was diagnosed measles. Jan. 11, pain in both ears. Drums incised and pus discharged. Jan. 20, much cough with râles over whole chest. Feb. 1, dulness in both lower lobes. Feb. 5, leucocytes 8,600. Temperature very irregular, varying daily from 97–103° F., pulse 80–110. On Feb. 7 rash had disappeared, throat not reddened. Dulness merging into flatness over left lower lobe with tubular breathing in that area. Elsewhere indefinite. Thoracentesis on the left side below the angle of the scapula gave 60 cc. of bloody fluid which contained Gram-positive insoluble cocci apparently streptococci. The sputum contained similar cocci and influenza bacillus. Blood culture on this day gave Pneumococcus Type IV. Feb. 8, patient very ill; temperature 104°. Lungs resonant anteriorly with large râles. Died Feb. 10, at 4 a.m. Autopsy Feb. 10, 10 a.m.

Anatomical Diagnosis: Bilateral lobar pneumonia.

Left pleural cavity.—Contains 800 cc. of greenish yellow fluid with shreds of fibrin. The pleural surfaces are shaggy and covered with a fine honey-combed layer of fibrinous exudate. *Right pleural cavity.*—Contains no excess of fluid; there are some fresh adhesions over the posterior surface of the lung which are easily broken through. There are also interlobar adhesions which are rather lax. *Left lung.*—The upper lobe is in general air-containing, although in its lower part there are a few yellowish opaque patches surrounded by hyperemic zones. The lower lobe is quite uniformly consolidated, the alveolar exudate projecting as minute granules which give the cut surface a reddish grey color. The septa are not conspicuous. The bronchi are somewhat reddened, the bronchial glands enlarged. *Right lung.*—The anterior portions of all the lobes are distended with air. The upper lobe is air-containing except in its lower portion where there is a patch of uniform consolidation. There are pretty dense interlobar adhesions. The middle lobe contains only a few small foci of consolidation which are grey and prominent. The lower lobe shows a rather peculiar distribution of the consolidation. There is a wedge-shaped area extending upward and backward from the hilum and about 3 cm. in width at its base at the pleura. There is also a large irregular area measuring about 10 by 5 cm. which extends through most of the lower and posterior part of the lobe. These are greyish red and uniformly consolidated. Between these and below the lower one there are air-containing portions of the lung. The bronchi are only slightly reddened and not thickened or prominent. The interlobular septa are rather conspicuous. The lymph glands at the hilum are large and soft. Other organs show no especial alteration.

The blood post mortem gave *Streptococcus hæmolyticus* and the influenza bacillus. Cultures from both lungs gave *Streptococcus hæmolyticus* alone.

Microscopic Examination.—The consolidated tissue from the left lower lobe shows a typical lobar pneumonia. The pleura is covered with a thin layer of fibrin with numerous leucocytes and innumerable cocci in pairs. The pleural membrane itself is hyperemic but not especially thickened or infiltrated and there is no

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trace of organization of the overlying fibrin. The interlobar spaces present the same appearance. The bronchi contain a purulent exudate with enormous numbers of cocci in pairs. There are also great numbers of influenza bacilli. There is a slight infiltration of their walls with leucocytes and a few mononuclear cells, but this is relatively inconspicuous. The alveolar walls are normal in thickness and are nowhere infiltrated with cells. The capillaries seem to be on the whole rather empty and compressed. The alveoli are closely packed with leucocytes. Those nearest the atria and bronchioles are especially full of these leucocytes, while in the peripheral parts of the lobule fibrin occupies a part of the space. The leucocytes are disintegrating and although in most places the nuclei are well preserved the cell outline is ragged or indistinct. Red corpuscles are scarcely seen. The leucocytes have acted as phagocytes and many of them appear as rounded packets of micrococci. The bacteria are numerous especially in the alveoli which are centrally placed and free of fibrin. These are rather elongated cocci in pairs arranged stiffly and suggesting pneumococci rather than streptococci. Their distribution is that of pneumococci also. The interlobar septa are rather wide and are infiltrated with fluid and fibrin. The blood vessels and lymphatics which run in these septa contain leucocytes and fibrin with many organisms. The bronchial glands show a great collection of large phagocytic cells in their sinuses which are much widened to accommodate them.

Other portions of the lung aside from the consolidated area show, especially in the lower lobe of the right side, a great deal of edema. The bronchi are in most places filled with leucocytes and there is a slight infiltration of their walls. In the alveoli which contain fluid there are great numbers of cocci. These are commonly collected about minute rounded spaces so that they lie in the fluid on the surface of these bubble-like spaces. Such spaces are no larger than a leucocyte and often form a network in the coagulated fluid contents of the alveolus. In most places the same stiff arrangement of the cocci in pairs is seen, but in some alveoli there are bacteria of different form. There are minute round cocci arranged in long wavy or twisted chains. These are evidently streptococci and distinguishable by their morphology even in the tissue. They are not abundant and the pneumococci seem well preserved so that it is remarkable that streptococci alone were recovered in cultures from the lung. Other organs show no especial alteration.

Case 36.—J. W., age 29 yrs. No history of measles. Entered hospital Jan. 19, 1918, complaining of dizziness and headache, pain in left side of chest, cough, and expectoration of blood-streaked sputum. Throat negative. Signs of consolidation in lower lobes of both lungs. Blood culture negative. Leucocytes 40,800. Urine shows faint trace of albumin, otherwise negative. Temperature 102–105° F., gradually falling to 98° at time of death. Pulse about 100, respiration 30–40. Sputum showed Pneumococcus Type I. Was given antipneumococcus serum Jan. 19. Feb. 1, feet became edematous. Insomnia on account of

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dyspnea. Urine shows albumin, pus cells, blood, and granular casts. Died Feb. 12, 1918. Autopsy Feb. 12, 1918.

Anatomical Diagnosis: Lobar pneumonia with encapsulated empyema (left). Serofibrinous pleuritis (right). Subacute pericarditis. Acute nephritis.

Left pleural cavity.—Contains a considerable quantity of thick greenish yellow pus which is encapsulated in several distinct and non-communicating pockets. The largest of these pockets containing about 300 cc. of pus lies between the anterior border of the lower lobe and the pericardium. The other pockets are between the lower lobe and the lateral chest wall. Posterior to the upper lobe there is another encapsulated empyema cavity containing 250 cc. of pus. Elsewhere the pleural cavity is obliterated by dense fibrous adhesions. *Right pleural cavity.*—Contains about 500 cc. of blood-stained fluid. The lung is collapsed and adherent over the posterior surface by fibrinous exudate. *Pericardium.*—The pericardial sac is obliterated by fresh fibrous adhesions except for two small pockets which contain blood-stained fluid. The heart shows no other abnormality. *Left lung.*—The pleura is thick and yellowish with abscess-like spaces in the substance. In places it is lifted up from the lung by accumulations of fluid. Both lobes of the lung are flabby and airless. In the upper lobe there is a small moderately firm but rather spongy area in the posterior part hear the hilum. In general the substance of the lobe is reddish grey in color and in the posterior part there is a grey patch of loose consolidation. There are no small areas of focal consolidation. The cut surface of the lower lobe is also greyish red, but there are a few hemorrhagic areas which measure 2 to 4 mm. in diameter and project above the surrounding lung tissue. The bronchi are very hyperemic, and the bronchial glands are very soft. *Right lung.*—The pleura is thickened and covered with a thin fibrinous exudate which, however, appears as a viscid, bloody fluid between the lung and the diaphragm. The lobes are all easily distended with air. On section the cut surface is greyish red in color and there are no areas of consolidation. Bronchial mucosa is reddened. Bronchial glands are not enlarged. *Kidneys.*—Right kidney measures 15 by 8 by 4.5 cm. The capsule strips off readily leaving a smooth greyish purple surface on which can be seen numerous small hemorrhages. On section the cortex measures 8 mm. in width, is dark greyish red and opaque, and is studded with numerous small hemorrhages. Glomeruli are visible as small dots. The mucosa of the pelvis is injected. The left kidney is quite similar.

Cultures from the pleural fluid gave Pneumococcus Type I and *Streptococcus hæmolyticus*. Those from the left lung gave the streptococcus alone.

Microscopic Examination.—The left lung shows in the consolidated areas a rather lax filling of the alveoli with leucocytes together with a ragged network of fibrin. There are enormous numbers of organisms, most of which lie free among the leucocytes. They are lanceolate diplococci and seem to possess a definite capsule. There is some infiltration of the bronchial and vessel walls and even of the alveolar walls, but it is chiefly with polymorphonuclear leucocytes, there being relatively few mononuclear cells. There is no marked thickening of the

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bronchial walls or infiltration of the interlobular septa. There is no organization of the intraalveolar exudate. Even in distant and relatively unaffected parts of the lung there is some infiltration of the alveolar walls with leucocytes. The pericardium shows a thick layer of fresh granulation tissue binding together the two layers. This is much infiltrated with leucocytes.

The kidney shows extensive changes in the glomeruli, tubules, and interstices. The glomeruli are large, their capillaries packed with nucleated cells, many of which are leucocytes. In the capsule of Bowman there are in some cases hyaline masses and strands which stain pink with eosin. In places the capillaries of the glomerular tuft are adherent to the parietal wall of the capsule. The epithelium of the tubules shows rather advanced degenerative changes. The tubules are in many places filled with blood and polymorphonuclear leucocytes. So too the interstitial tissue between the tubules of the cortex is in many places greatly widened and infiltrated with leucocytes.

Case 40.—B. M. G., age 28 yrs. No history of measles. Caught cold on Jan. 29, 1918, and had a chill followed by fever and vomiting. Felt very much nauseated for several hours. Pain in the right side of chest. Entered the hospital Jan. 30, with dulness and diminished breath sounds in the right chest behind. Left side apparently normal. Sputum bloody with Pneumococci Type IV. Leucocytes 30,000. On Feb. 8 temperature fell to normal, but the next day it rose again, and from that time to death showed great variations. Patient very ill and unconscious. Stiffness of neck and arms. Death Feb. 13, 1918. Autopsy Feb. 14, 1918.

Anatomical Diagnosis: Lobar pneumonia with fibrinous pleuritis.

Left pleural cavity.—Contains 150 cc. of blood-stained fluid. There are old fibrous adhesions over the whole lung posteriorly and between the lobes. *Right pleural cavity.*—Entirely obliterated by light fibrinous adhesions which are easily torn through. There is no fluid. *Left lung.*—Air-containing throughout, but a few bronchi in the posterior portion of the upper lobe contain plugs of exudate. Their walls are thick and greyish. *Right lung.*—The pleural surface is dull and covered with a thin fibrinous exudate. On section the lung is found to be uniformly consolidated throughout and grey in color except for a few lobules in the central portion of the lower lobe which are red and loosely consolidated. The alveoli are everywhere filled with plugs of exudate which project above the cut surface giving it a roughened appearance. The interlobular septa are rather conspicuous in the lower lobe.

Microscopic Examination.—The left lung shows no alteration except the bronchial changes in the upper lobe which prove to be tuberculous. Sections through the consolidated right lung show a perfectly uniform filling of the alveoli with masses of exudate composed of leucocytes and fibrin. The fibrin has become compact; the leucocytes are disintegrated. There are also desquamated epithelial cells and some large phagocytes, which contain cell fragments. There are many cocci in short chains which are presumably pneumococci although no cultures

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were made and some of them look like streptococci. The walls of the alveoli are not thickened and the finer structure appears unchanged. The pleura is thickened and vascularized and is covered with a thin layer of fibrin. In it there are lymphatics which contain masses of leucocytes and large phagocytes. The interlobular septa are wide and dense.

Bronchi and blood vessels show in many cases a definite mononuclear infiltration of the walls. Nevertheless in most of the smaller vessels the infiltration is largely in the adventitial lymphatics and is composed of polymorphonuclears. Near the pleura the exudate in many alveoli has undergone organization.

Case 45.—J. K. S., age 19 yrs. Measles when a child. No eruption lately. Onset Jan. 17, 1918, with a chill, cough, and expectoration of tenacious, blood-streaked sputum. Fever and weakness. Entered the hospital Jan. 18, 1918, with painful dyspnea and dulness over lower lobes of both lungs posteriorly. Leucocytes 30,000. Temperature 101–105° F., pulse 100–150, respiration about 50–60. Sputum showed Pneumococcus Type III (?). On Jan. 25 he apparently had a fall of temperature by lysis but were still very sick, coughing up purulent material. There was still dulness posteriorly over both lungs with diffuse crepitant râles. Aspiration negative on both sides. Steadily improved for the next week, but on Feb. 1 there were still some dulness and the same crepitant râles. Sputum now showed *Streptococcus hæmolyticus*. Feb. 12, lungs fairly clear throughout. There are a few spots of dulness with crepitant râles, but the breath sounds are mostly vesicular. There was a sudden rise in temperature to 106° followed by a fall to 97° on the 14th, when he lapsed into coma and died with symptoms of extreme dyspnea. Death Feb. 18, 1918, 10 a.m. Autopsy Feb. 18, 1918, 11 a.m.

Anatomical Diagnosis: Indurative and organizing pneumonia with abscesses and pleural adhesions. Acute aortic endocarditis. Bilateral abscesses of rectus abdominis. Acute splenic tumor. Duodenal ulcer.

Right and left pleural cavities.—The cavities contain no fluid. The surfaces are bound together everywhere by organized adhesions which are thin, delicate, and veil-like. *Heart.*—Pericardium is normal. The heart is not enlarged, contains only postmortem clot. The endocardium is smooth throughout except over the aortic valve. The right coronary and posterior leaflets are occupied by large reddish yellow masses which in each case bulge in rounded forms both into the sinus and into the ventricle penetrating the leaflet. The right coronary orifice is not involved and the coronary vessels are normal throughout. The other valves are delicate and competent. The heart muscle is greyish red and uniform in appearance. *Left lung.*—The lung is small but very cushiony throughout as though everywhere air-containing. The bronchi exude a thick purulent fluid. On section the tissue is yellowish brown in color and in general air-containing, but through the lower lobe there is a network of greyish yellow strands which are irregular in outline and firmer than the surrounding tissue. In places these are rather translucent, in other places much more opaque than the adjacent tissue. The upper

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lobe is more uniformly air-containing, but it too shows a few firm patches like those in the lower lobe. These are not specially related to the bronchi which are practically normal in appearance. *Right lung.*—This lung is in general air-containing, but there are scattered through the whole organ such strands of condensed tissue as form a network in the left lung. This particular appearance is more distinct after the lung has been hardened when there appear normal spongy portions in the rather small meshes of the close network of denser tissue. This denser tissue has not the appearance of a pneumonic consolidation but suggests the possibility of organization and contraction of an old pneumonic exudate. The upper lobe contains in addition a small group of abscesses each measuring 3 to 5 mm. in diameter and filled with yellow pus. In the anterior part of the lower lobe the tissue is entirely solid, dense, and grey. There are two small abscesses in this area. *Stomach and duodenum.*—Just below the pylorus there is an ulcer about 1 cm. in diameter in the mucosa of the duodenum. The margins are not indurated; the pancreas is not adherent to the base of the ulcer. *Rectus abdominis muscle.* —There is an abscess measuring 1 by 4 cm. in the substance of each rectus muscle about the junction of middle and lower thirds. These abscesses are exactly symmetrical in position. They contain a thick, sticky green pus and are lined by a yellowish wall which is stained brown in its deeper portions.

Cultures at autopsy gave the following results: Right lung, *B. influenzæ*, *Staphylococcus aureus* (hemolytic), *Streptococcus hæmolyticus*, and no pneumococcus. Heart valve and abscess in rectus muscle, Pneumococcus Type I.

Microscopic Examination.—The lungs show practically the same changes. The pleura is slightly thickened and vascular with some infiltration of wandering cells. There are on the surface remains of dense fibrin and groups of the original lining cells of the pleura.

The interlobular septa are not especially thickened. The bronchi show practically no changes in their walls although most of them are filled with leucocytes. The epithelium is in general intact and the connective tissue and muscular layers of the wall are compact and show very few wandering cells.

On the other hand, the alveolar walls in most places are extraordinarily thickened, not by infiltration with mononuclear cells but by a new formation of connective tissue. There are, it is true, some mononuclear wandering cells in the substance of these walls and many of them are very large and loaded with yellow pigment. The epithelium is in general complete but much thickened so as to be almost cubical in many places. The alveoli are usually empty but there are places in which they still contain leucocytes and other more extensive places in which they are filled by an organized tissue. This organization of old exudate is not very widespread, however. Such changes in the lung are not uniformly distributed, but alternate with areas in which the alveoli are overdistended with air but are otherwise normal. The exudate both in the bronchi and alveoli contains pneumococci, very abundant influenza bacilli, and occasionally a coarse streptothrix.

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Blood vessels and lymphatics are inconspicuous.

In certain sections of the lung there are found large abscesses with old compact masses of fragmented leucocytes forming the center within a dense wall of granulation tissue.

Case 46.—F. W. S., age 23 yrs. Had measles 10 years ago according to his own account. Had no doctor. Began Feb. 5 with headache, conjunctivitis, coryza, sore throat, and malaise. On Feb. 6 chills and fever with red papular eruption on chest and face next day. Admitted to hospital Feb. 7. On Feb. 10 had a chill, vomiting, and headache. Temperature 104° F. Feb. 14, signs appeared in lungs for the first time. There was a period of normal temperature between the measles and the pneumonia. Feb. 15, uncomfortable, breathless with a grunt and cyanosis. Dulness over left back and axilla, breath sounds tubular over tip of lower lobe. Bronchophony and whispered pectoriloquy here. Tactile fremitus diminished. Died Feb. 18, 11 a.m.

Sputum on Feb. 15 shows Pneumococcus Type I, also *Streptococcus hæmolyticus*. Blood culture on that day gave Pneumococcus Type I. On Feb. 16 cultures of fluid aspirated from the chest gave Pneumococcus Type I and *Streptococcus hæmolyticus*. Thought to have lobar pneumonia with empyema and secondary streptococcus infection. Autopsy Feb. 18, 1 p.m.

Anatomical Diagnosis: Pneumonia with abscess formation and empyema. Fibrinopurulent pericarditis.

Left pleural cavity.—Contains an enormous amount of fluid which is olive-green in color, turbid with great flakes of fibrin floating up from the injected pleural surface. *Right pleural cavity.*—Contains no fluid; the pleural surfaces are smooth and glistening. *Pericardium.*—Contains 300 cc. of turbid fluid with floating shreds of fibrin. The walls are thickly studded with small hemorrhages and covered with a loose fibrinous exudate. *Left lung.*——Completely collapsed and flattened against the mediastinal tissues; is flabby and soft, except in the upper part of the lower lobe where there are several firm masses, one of which is necrotic and covered by yellow necrotic pleura. On section it is found that there is an abscess about 12 mm. in diameter in the upper posterior part of the lower lobe. About it is a clearly outlined zone of uniform greyish consolidation. The rest of the lower lobe is collapsed. In the upper lobe the interlobular septa are prominent but there is no consolidation. Bronchi contain purulent fluid but the walls are not thickened nor are the bronchi dilated towards the pleura. *Right lung.*—Air-containing throughout and normal in appearance. The adrenals are greatly swollen and have lost the distinctness of their zonal marking.

Microscopic Examination.—The pleura over the left lung is thickened by the formation of granulation tissue which is overlaid by a thin but dense layer of fibrin. The interlobular septa are not very conspicuous, although slightly thickened and infiltrated with fibrin and cells. The tissue under the pleura is consolidated, each alveolus being packed with dense fibrin which contains but few cells. These are mostly red corpuscles, desquamated epithelium which is deeply pigmented,

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and leucocytes. The alveolar walls are greatly thickened by infiltration with various sorts of cells, chiefly mononuclears which act as phagocytes. This dense consolidation extends for a considerable depth. Even where the lung becomes insufflated it appears that the air is only forced into partly consolidated, partly collapsed tissue. The bronchi contain a purulent exudate, but their walls are not much altered from normal, and very slightly infiltrated.

The lymphatics in the bronchial and vessel walls are distended with leucocytes, fibrin, and bacteria. There is a fresh pericarditis with hemorrhages under the pericardial lining cells and a little fibrinopurulent exudate.

Cultures from pleural fluid, pericardial fluid, both lungs, and blood gave *Streptococcus hæmolyticus*. No pneumococcus was found in material from these five sources.

Case 51.—J. L. A., age 35 yrs. Had a cold for several days and was admitted to the hospital Feb. 15, 1918, with chill, fever, and vomiting. Dulness over right lower lobe with crackling râles. No tubular breathing. Faint pleural rub near the right nipple. On Feb. 17 there was a crisis and the temperature sank to normal from 103°. Patient remained in good condition until Feb. 24 when he had a chill followed by severe pain in the right side. There were dulness and diminution of breath sound in this region. Sputum contained pneumococcus. On Feb. 27 the tenacious bloody sputum contained Pneumococcus Type II, with influenza bacilli. Mar. 1, patient was very sick, with abdominal distension. Tubular breathing and râles on right side. Blood culture gave Pneumococcus Type II. Sputum gave the same organism. Aspiration of thorax was negative on Mar. 2 and 3. Patient cyanotic; râles over entire chest. Tubular breathing over right lower lobe only. Died Mar. 4, 1918, at 2.15 a.m. Autopsy Mar. 4, 1918.

Anatomical Diagnosis: Lobar pneumonia (right lower lobe) with anemic infarctions. Fibrinopurulent pleuritis. Acute peritonitis. Diphtheritic colitis.

Left pleural cavity.—Contains a few cc. of turbid fluid. The surfaces are fairly smooth except on the posterior portion of both lobes where the lung is collapsed and there are numerous hemorrhages on the surface. *Right pleural cavity.*—Obliterated by fresh fibrinous exudate which is especially thick over the upper part of the lung where it contains some fluid. There is no free fluid but it is held in the meshes of the fibrin. The surface of the diaphragm is deeply injected. *Pericardium.*—The pericardium contains about 100 cc. of slightly turbid fluid. There are a few punctate hemorrhages on the heart but the surfaces are smooth and glistening. *Peritoneum.*—The hepatic flexure of the colon is adherent to the liver, and in this region the peritoneum has lost its gloss and there is a collection of purulent fluid. The appendix and pelvic organs are bathed in purulent fluid. There is less fluid on the left side and the peritoneal surfaces are glossy. There is no obvious source for this infection. The mucosa of the intestines is normal throughout except for a few areas of diphtheritic exudate in the region of the ileocecal valve, which stand above the surrounding mucosa and are out-

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lined by hemorrhage. *Left lung.*—The lung feels soft throughout although there is some collapse in its posterior part. It was readily insufflated artificially and on section the tissue is normal in appearance throughout. There is no thickening of the bronchi. *Right lung.*—The organ is voluminous and heavy. The upper lobe is soft and collapsed and so is the middle lobe except in the anterior part where it is air-containing. The lower lobe is distended with exudate and is solid. The bronchial glands are enlarged and the bronchi contain a purulent exudate. The upper and middle lobes are insufflated readily and normal in structure. The lower lobe on section shows a uniform consolidation in which the alveoli are filled with an exudate of dark reddish grey color. There is no thickening of the bronchial walls and no focal character to the consolidation. There is a firm grey area at the lower margin and the blood vessel passing to this area is thrombosed. There are several patches just beneath the pleura in the more posterior part of the lobe, which correspond sharply with the outlines of lobules and in which the consolidated tissue is paler and mottled. Over one of these the thick yellow fibrinous exudate is thinned out so that the opacity of the area shows through. All such patches come up to the surface of the lung and are pale grey, sometimes with reddish central portions or small areas of softening. The blood vessels supplying these areas appear to be thrombosed. The interlobular septa are not widened, but there are some beaded distended lymphatics in the lower part of the consolidated lobe. These are rendered conspicuous by their opaque yellow contents.

Cultures at autopsy from the lung showed Pneumococcus Type II atypical with *B. influenzæ*; peritoneal and pericardial fluids contained Pneumococcus Type II atypical in pure culture. The blood gave Pneumococcus Type II atypical with a Gram-negative colon-like bacillus.

Microscopic Examination.—The consolidated right lung shows the typical lesions of lobar pneumonia. The pleural exudate is of fibrin not organized. The pleura is not thickened and the original layer of pleural lining cells is still distinguishable. The interlobular septa are wide, infiltrated with fluid and a network of fibrin. There are many polymorphonuclear leucocytes and some mononuclear cells in the meshes of the fibrin. The lymphatics in these septa are enormously distended and plugged completely with clotted masses of leucocytes, blood, and mononuclear cells among which rather numerous pneumococci can be seen. The lymphatics in the pleura and in the adventitia of blood vessels and of bronchi are also distended with the same material, but they are not such huge beaded channels as those related to the septa.

The bronchi contain leucocytes and fibrin with pneumococci and influenza bacilli, but their walls are not thickened or markedly infiltrated nor is their epithelium destroyed. The alveoli are uniformly filled with a network of fibrin with leucocytes, red corpuscles, and great numbers of pneumococci. Their walls are not thickened or infiltrated, although occasional leucocytes are found there. There are several blood vessels which are completely thrombosed and the areas of lung tissue ordinarily supplied by them are, with their contained exudate,

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completely necrotic. These represent anemic infarctions in the consolidated lung. The bronchial glands are enlarged and contain in their sinuses phagocytic cells and pneumococci.

Case 186.—W. F., age 29 yrs. Began with cough, general malaise, and pain in chest, and was admitted to the hospital on May 2, 1918. Bubbling râles were found in both lungs. On May 8 there was evidence of meningitis, and 50 cc. of spinal fluid were aspirated, 45 cc. of antimeningococcus serum being injected. On May 11 there were signs of consolidation in the left lower lobe. On May 12 patient was irrational and cyanotic. 50 cc. of fluid were aspirated from the left chest. Sputum contained Pneumococcus Type I and influenza bacillus on May 11. Died May 12, 1918. Autopsy 20 hours after death.

Anatomical Diagnosis: Lobar pneumonia (left lung) with fibrinopurulent pleurisy. Acute serofibrinous pericarditis.

Left pleural cavity.—The cavity is practically obliterated by a great mass of greenish yellow fibrin which is thick and shaggy and in the interstices of which there is a large quantity of turbid greenish fluid. This accumulation is chiefly between the lung and the pericardial sac. The lung is bound to the costal pleura by fresh light fibrinous adhesions. There are about 160 cc. of fluid in the space between the lung and the pericardial sac, but the rest of the pleura contains relatively little fluid. The surfaces, where free, are covered with greenish fibrin in a thin layer. *Right pleural cavity.*—Contains no fluid. The surfaces are smooth and glistening. *Pericardial cavity.*—Contains 50 cc. of turbid fluid with shreds of fibrin. The pericardial lining membrane is congested, its surface dull, and covered with a thin exudate of fibrin. *Mediastinal tissue.*—Infiltrated with yellow purulent exudate. At the region of the lower end of the thymus there is an abscess-like accumulation of pus. *Left lung.*—The lung is large and heavy with its lobes glued together by fibrin which extends over the surfaces as described. The upper lobe is air-containing in its anterior and upper part, but in the region of the hilum and near the cleft between the lobes there are greyish translucent branching areas of consolidation. The bronchi are thickened and reddened, but it is not clear that these consolidations are definitely peribronchial. In the lower lobe there are two definite areas of consolidation between which the lung is collapsed and contains only indefinite nodular foci of consolidation. One of these larger areas occupies the upper posterior portion, the other the anterior lower part. They are reddish grey and uniform, showing a granular surface from which a plug of exudate projects from each alveolus. The bronchial glands are large, soft, and edematous, and contain some old yellowish nodules. *Right lung.*—Everywhere air-containing except for a few small patches of greyish red consolidation in the lower part of the upper lobe. *Pharynx and larynx.*—Pharynx, epiglottis, and larynx slightly congested. There are no ulcerations in the vocal cords or elsewhere in the larynx. The trachea is slightly reddened.

Cultures from the heart's blood, left lung, and pericardium gave Pneumococcus Type I. A culture from the left pleura showed *Streptococcus hæmolyticus.*

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Microscopic Examination.—The left lung shows a thick layer of fibrin on the pleural surface with abundant Gram-positive cocci in short stiff chains scattered throughout. Many of these are in phagocytic cells. The pleura itself overlaid with a dense exudate of fibrin is edematous, slightly thickened, and spread open into meshes and remarkably hyperemic. It appears that there is the beginning of organization of the overlying exudate, although the proliferation of connective tissue cells has barely begun. The pleural lining cells are almost all gone; a few can still be seen. The interlobular septa are quite inconspicuous. The lymphatics in the pleura are filled with fibrin and cells with few bacteria. They are not easily found in the substance of the lung. The bronchi are filled with purulent exudate; their walls are slightly infiltrated with mononuclear cells. The alveolar walls are nowhere thickened or infiltrated. Their cavities are filled with an exudate of leucocytes, red corpuscles, and fibrin. There are numerous Gram-positive diplococci in places in the alveolar exudate, but almost all of them are enclosed in leucocytes and are apparently partly disintegrated. They, like those seen in the superficial layers of the pleural exudate, look like pneumococci. In addition to these there are in the bronchial exudate great numbers of influenza bacilli. In another section from the left lung there is the same condition of the pleura, but the alveoli are filled not with a fresh exudate of leucocytes but either with fluid or with a dense exudate of fibrin in which are entangled red corpuscles and a few mononuclear cells and leucocytes. These plugs of fibrin are outlined in many cases by a single layer of flat epithelial cells which have grown over them from the alveolar wall. The alveolar walls are thickened by an infiltration with leucocytes. In places the epithelium is greatly proliferated and several mitotic figures can be seen in these cells in a single alveolus. They grow until the alveolus is half filled with a mass of epithelium. In this region the walls of the vessels are somewhat infiltrated with mononuclear cells, but those of the bronchi are not much thickened. Enormous numbers of bacteria are found on the surface of the pleural fibrin, but none in the alveolar cavities.

This is a peculiar condition since certain parts of the consolidated tissue show the alveoli almost but not quite filled with a compact fibrillated mass clothed in a layer of epithelial cells in which the cells are indistinct and in which no bacteria are found, while other areas are filled with exudate containing bacteria. The proliferation of the epithelium recalls the epithelial giant cells described by Hecht in the lungs of children.

Case 188.—D. W., age 21 yrs. No history of measles. Began gradually about May 3, 1918, with a cough and pain in chest. Drilled for 2 days when pain became more severe. Admitted to hospital May 7 when he had a few crepitant râles in the left lower lobe. On May 11 there were tubular breathing, crepitant and moist râles in the right upper lobe, and few râles in the left lower lobe. On May 13 it was evident that there was consolidation of the right upper and middle lobes with many râles. Diagnosis of lobar pneumonia, left lower, and right upper and middle lobes. Died May 14, 1918, 1.05 a.m. Autopsy May 14, 1918.

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Anatomical Diagnosis: Lobar pneumonia involving whole right lung (fresh). Organizing lobar pneumonia (left lower lobe). Fibrinous pleuritis. Acute nephritis.

Left pleural cavity.—There is a fibrinous exudate over the whole lower lobe which binds it to the costal pleura. This extends between the lobes and a short way on the upper lobe; the remaining pleura over the upper lobe is smooth and without adhesions and contains no excess of fluid. *Right pleural cavity.*—The whole cavity is obliterated by a fresh fibrinous exudate which glues the surfaces together. There are a few old adhesions about the apex of the lung. There is no accumulation of fluid. *Left lung.*—The upper lobe is uniformly air-containing and of normal texture. The lower lobe is nearly solid but there are small spongy patches distributed throughout. These alternate with greyish red irregular areas of solid lung which show a rough surface with projecting alveolar plugs. The bronchi are lined by an opaque ragged layer. In several places but especially near the hilum there are large branching opaque yellow lines which look like obstructed lymphatics. *Right lung* (*Fig. 51*).—Large and heavy and consolidated except in the anterior margin of the middle and lower lobes. It is covered with a thin fibrinous exudate more abundant between the lobes which are glued together. The bronchial glands are very large, pigmented, and flecked with pale grey opacities. The upper lobe on section shows a few small scattered patches of spongy air-containing lung; these patches amount to only a few alveoli in each case. They are separated by rather mottled greyish red areas of consolidation which are flecked in places with hemorrhages. These areas are practically confluent and continuous throughout. The bronchi contain a grey exudate and in places their lining walls are opaque and yellowish red. The middle lobe is more uniformly consolidated, paler than the upper, and with more definite alveolar plugs. It too is flecked with hemorrhages. The lower lobe like the middle is uniformly solid and no spongy areas are seen. It is paler than the upper lobe and does not contain so many hemorrhages.

Microscopic Examination.—The right lung shows in its consolidated part a pleura covered with dense fibrin. On the outer surface the covering cells are largely destroyed but there is very little evidence of organization. In the interlobar space, however, the lining pleural cells are well preserved in most places. Nevertheless, definite organization of the exudate is going on. The interlobular septa are not conspicuous and lymphatics are scarcely to be found in the sections. The bronchi contain a purulent exudate. Their walls are not thickened or infiltrated. The alveolar walls are not thickened. The alveoli contain a rather uniform dense exudate of polymorphonuclear leucocytes, red blood corpuscles, and fibrin. Blood is very abundant in places. In other areas edema predominates. The exudate both in the bronchi and alveoli is loaded with bacteria. The Gram-positive cocci are usually free and are morphologically identical with pneumococci. There are great numbers of minute Gram-negative bacilli, most of which are contained in leucocytes, in the protoplasm of which they are closely packed. These appear to be influenza bacilli.

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The left lung presents a different appearance and it is difficult to decide how this should be interpreted. The consolidation is patchy, with areas which contain air. The pleura is thickened by a layer of granulation tissue over which there is fibrin. The interlobular septa are not prominent. The bronchi are filled with a purulent exudate; their walls are slightly spread apart and contain a few wandering cells with leucocytes and mononuclear cells. Some of the bronchi show a distinct overdistension of the blood vessels, but the changes are in general slight. The alveolar walls are not thickened or infiltrated with mononuclear cells. The alveoli are not filled with an exudate of polymorphonuclear leucocytes as in the right lung, but contain fluid, red blood corpuscles, desquamated epithelial cells, and dense masses of fibrin containing few cells but overgrown and almost completely covered by epithelium. Such masses are partly replaced by new connective tissue. There are some areas in which the alveoli contain leucocytes, but throughout most of the lung the condition is as described. Possibly it represents a much later stage of the lobar pneumonia caused by the pneumococcus than that seen in the right lung, but it is also possible that these changes may depend upon the influenza bacillus.

The kidney shows a general cloudiness of the cells of the epithelium of consolidated tubules, although their free borders are well preserved. There are several glomeruli in each section in which the capillaries are plugged with hyaline thrombi. In the capsules of all the glomeruli there is a mass of bubble-like coagula and in those which have the thrombosed capillaries there are a few leucocytes. The tissue surrounding these glomeruli is infiltrated with red corpuscles and leucocytes. Some of the tubules contain casts and a few polymorphonuclear leucocytes.

There is little that requires comment in these cases. Most of them were from the Texas epidemic, which is perhaps to be accounted for from the fact that those studies were made in February and March, while the Iowa epidemic was studied in May.

The cases of lobar pneumonia are described here not because they are extraordinary in any way, but chiefly to show the proportion which they bear to the others and to emphasize the contrast between the anatomical lesions produced by the different organisms.

The distribution of these organisms has already been mentioned. It was Ribbert's idea that in lobar pneumonia one might recognize a lobular arrangement of the exudate with most compact fibrin in the alveoli adjoining the interlobular septa, while the greater number of leucocytes and more especially of pneumococci was to be found in the central portions of the lobule and in the bronchus. This is true to some extent, although the pneumococci are far more uniformly dis-

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tributed throughout the alveoli and through the whole thickness of the pleural exudate than are streptococci. The latter organisms keep to the bronchial contents and the surfaces of the pleural exudate in interstitial bronchopneumonia and are scattered more like pneumococci in the lobular form. But both pneumococci and streptococci quickly gain the lymphatics and distend them with the resulting exudate which clots. In lobar pneumonia as in the streptococcal form these lymphatics become very prominent in their course from the pleura as beaded yellow channels.

In several cases in which there was definite lobar pneumonia and in which blood cultures during life showed the presence of pneumococci (Case 33), or when sputum and pleural fluid contained them (Case 36), or sputum, blood, and pleural fluid (Cases 45 and 46), the cultures from lungs and other sources at autopsy failed to show them and *Streptococcus hæmolyticus* grew instead. It appears from repeated experiences of this kind that the pneumococcus must quickly die out or be overgrown by the streptococcus, or one may find it, as in Cases 186 and 188, in the process of being overgrown.

Curious changes occur in the exudate itself if the first stages of the disease are survived. In Case 25, which was of only 8 days duration, the pneumonia was thought to be in a stage of resolution. This seems questionable, but at any rate few pneumococci could be found in sections, although the fibrin still stained well and they were isolated in culture. But in this lung the infiltration of the alveolar walls with polymorphonuclear leucocytes and the upheaval of the epithelial cells are remarkable. Of a different character are the changes in Case 45 in which the pneumonia has left the alveolar walls thickened with fibrous tissue in certain strand-like areas, and the alveoli themselves filled with organized exudate in the form of fibrous bands. The presence of abundant influenza bacilli must be remembered.

Organization is advanced in one of the lungs of Case 188, and in Case 186 there are alveoli partly filled with dense fibrin from which bacteria have disappeared and nuclei faded. In Case 186 there are in places striking evidences of the proliferation of the epithelium which forms great protoplasmic masses only faintly divided into cells and studded in places with mitotic figures.

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One of the most striking lesions, which may be common enough in any great series, is shown in Case 51 in which the cultures show throughout Pneumococcus Type II. In this uniformly consolidated lung there are many thrombosed blood vessels and as many anemic infarctions which extend to the pleura. They are actual infarctions because the circulation of the lung is embarrassed, and anemic because the lung has become firm like the kidney and there is no longer a chance for blood to ooze into the dead area from adjacent regions.

No unusual changes were found in the other organs in connection with this form of pneumonia, although there were pericarditis, endocarditis, peritonitis, and in one case abscesses of the rectus abdominis.

5. *Lobar Pneumonia Combined with Interstitial Bronchopneumonia.*

Case 21.—A. A. McL., age 22 yrs. Entered hospital Jan. 7, 1918, with fever, cough, and sore throat. Conjunctivæ injected, no rash, throat clear. Jan. 8, throat very red, marked conjunctivitis, but no rash. Jan. 10 and 11, cough with much expectoration, nausea, and vomiting. Chill and epistaxis. Had acute bronchitis since Jan. 1, otitis media Jan. 25. Jan. 26, there were dulness over the upper right lobe and râles over the entire chest. Very ill until Feb. 4 when he died. Temperature 100–104° F., pulse 100–120, respiration 24–30. Much delirium and vomiting. Leucocytes 25,600. Autopsy Feb. 5, 1918.

Anatomical Diagnosis: Bilateral lobar pneumonia. Bilateral interstitial bronchopneumonia. Fibrinopurulent pleuritis.

Left pleural cavity.—Free from fluid. Surfaces dulled by thin fibrinous exudate with minute hemorrhages. *Right pleural cavity.*—Contains a little viscid yellow fluid. *Left lung (Fig. 52).*—There is an area of consolidation which occupies the posterior part of the upper lobe. The lower lobe is partly collapsed, partly air-containing, the surface greatly injected and flecked with hemorrhages and covered with a fibrinous exudate. On section the upper lobe with the exception of a small part of the mesial surface is uniformly consolidated. The lower lobe shows on section numerous greyish white minute areas of consolidation distributed in groups of two or three, several being found in each lobule. These correspond with the terminal bronchioles. *Right lung.*—The upper lobe contains a large area of uniform consolidation in which each lobule is sharply outlined and shows each alveolus filled with exudate. Throughout the lower part of the lung there is atelectasis. In this area each interlobular septum is quite distinct and there are numerous minute areas of consolidation in each lobule. These correspond in position with the terminal bronchioles. The same condition is distinctly visible in the lower part of the upper lobe and may be traced into the area of lobar consolidation. The nodules are numerous throughout the remainder of the lung.

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Microscopic Examination.—The lungs are practically alike. In the sections which pass through the area of lobar pneumonia the pleura is not thickened. The overlying fibrin is not organized and the pleural lining cells are still visible. This is true over the portions of the lung occupied by the interstitial bronchopneumonia, but the pleura is distinctly more vascular and the fibrinous exudate thicker. In the area of lobar consolidation the bronchi contain an exudate of leucocytes; their walls are somewhat infiltrated with mononuclear cells. The adjacent and also distant alveoli are uniformly filled with the characteristic exudate of pneumococcus pneumonia. The walls are not definitely thickened or infiltrated. It is not really possible to recognize areas of interstitial bronchopneumonia embedded in the area of lobar pneumonia, although at the margin where the two conditions join one another it is true they overlap somewhat. The alveolar exudate contains many organisms, probably pneumococci, which are in pairs or short stiff chains scattered evenly throughout. Many of these are enclosed in phagocytes. No organization of this exudate has occurred. The interlobular septa are wide and edematous with a loose network of fibrin and many leucocytes and mononuclear cells. There are a few bacteria and often these appear to be streptococci in long flexible chains. The lymphatics injected from the pleura with Berlin blue run in these septa and are often plugged with thrombi rich in leucocytes. There are no great numbers of bacteria to be seen there. The blood vessels have walls somewhat thickened by an infiltration of mononuclear cells.

As one passes from the area of lobar pneumonia the whole character of the pulmonary alteration changes. The bronchi become conspicuous from the greatly increased thickness of their walls. They are still filled with leucocytes and debris of epithelial cells with streptococci, but the walls are very hyperemic and greatly thickened by the infiltration of mononuclear cells. This extends to the walls of the neighboring alveoli. Such alveoli are filled no longer with a delicate network of fibrin supporting uniformly distributed polymorphonuclear leucocytes, but are found to contain dense plugs of pink-staining fibrin surrounded by mononuclear wandering cells and desquamated epithelium. Streptococci are rarely found there. But organization has occurred everywhere and has advanced so that there are whole patches of the lung in each alveolus of which the exudate is replaced by vascular connective tissue which has retracted and has been covered by alveolar epithelium. The same is true in the bronchi although the connective tissue lies uncovered there in the midst of the exudate. Most of the lung is atelectatic, but the parts intervening between the peribronchial nodules can be blown up with air.

Pneumococcus Type IV and *Streptococcus hæmolyticus* were recovered from the lungs and from the heart's blood.

Case 23.—F. L. G., age 18 yrs. Taken sick Jan. 15 with cough and pain in left chest and fever. Entered hospital Jan. 19, 1918. Dulness over left lower lobe with tubular breathing and râles. Aspirated Jan. 31, and pus removed from left pleura. Resection of rib Feb. 1. Died Feb. 5. Autopsy Feb 5.

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Anatomical Diagnosis: Interstitial bronchopneumonia with empyema (left lung). Lobar pneumonia (right lung).

Left pleural cavity.—Over the 6th left rib in the anterior axillary line is an operation wound 7 cm. long from which projects a rubber tube. A piece of rib has been removed. The pleural cavity is entirely obliterated over the anterior half by light fibrinous adhesions. The posterior part of the pleura forms a cavity which extends to the vertebral column and contains a small quantity of purulent material. The mediastinal tissues are very edematous. *Right pleural cavity.*—Contains a small amount of fluid. The surfaces are covered with a thin fibrinous exudate. *Left lung.*—The lung is collapsed and adherent to the diaphragm where it encloses a pocket of 100 cc. of greenish yellow pus. The surface of the lung is covered with a yellow fibrinous exudate which binds the lobes together. In the posterior portions of both lobes, which are much collapsed, there are numerous greyish red foci in the centers of which bronchi are seen filled with purulent exudate. Other reddened areas 2 mm. in diameter seem not to be related to the bronchi. In the upper and posterior part of the lower lobe there is a grey area of consolidation in which each alveolus contains a plug of exudate. *Right lung.*—The lower lobe is covered with a thin fibrinous exudate while the surface of the upper lobe is smooth. The upper lobe is air-containing throughout, and there are no foci of consolidation. The lower lobe except for the anterior margin is uniformly consolidated. It is grey, firm, and airless and from each alveolus a plug of exudate projects. The lymph glands are moist and swollen.

Microscopic Examination.—The left lung presents the typical appearance seen in interstitial bronchopneumonia. The pleura is greatly thickened and appears as a layer of granulation tissue with overlying dense fibrin. Much of the lung substance is collapsed. The bronchi are conspicuous because they are filled with leucocytes and desquamated columnar epithelium. There are many influenza bacilli among these cells. The walls are greatly thickened and hyperemic and densely infiltrated with lymphocytes, plasma cells, and mononuclear wandering cells of other forms. The adjacent alveolar walls are similarly thickened in the neighborhood of bronchi, vessels, and interlobular septa. Their epithelium is partly desquamated and they contain these cells as well as the mononuclear wandering cells. Where fibrin is found in the alveoli it is not in a delicate network but in dense masses. Organization is well advanced and dense strands of vascularized tissue are found in the bronchi and in the alveoli. In the alveoli hemorrhage is not a prominent contributor to the exudate. There are some red corpuscles but far more of a formless coagulated fluid. The interlobular septa are greatly widened, and where lymphatics are seen they are packed with mononuclear cells and leucocytes.

Sections through the consolidated portions of the lower lobe of the right lung show a thin pleura with an overlying layer of fibrin showing no indication of organization. The bronchi contain an exudate of leucocytes; the epithelium is in-

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tact or retracted in a ring from the walls. There is no organization of the exudate. The walls of the bronchi are very slightly infiltrated with leucocytes and so too are many of the alveolar walls. It is striking that in this lung the polymorphonuclear leucocytes invade the alveolar walls, while in the opposite lung the mononuclear cells do so. The alveolar exudate is composed of leucocytes and fibrin. The latter is rather contracted and dense. Many of the alveoli contain fluid. Bacteria which are Gram-positive lanceolate diplococci of considerable elongation are numerous and uniformly scattered throughout the exudate. The influenza bacilli are also present. The interlobular septa are inconspicuous.

Bacteriological cultures show *Streptococcus hæmolyticus* in both blood and lung. Nevertheless it seems clear that the bacteria which have caused the lobar pneumonia in the right lung are pneumococci, both from the anatomical character of the lesion and the morphology of the organisms themselves together with their peculiar distribution.

Case 31.—J. D. W., age 22 yrs. Began Jan. 14, 1918, with headache, sore throat, coryza, and conjunctivitis. Rash appeared on Jan. 18 when he entered the hospital. Difficulty in breathing developed shortly afterward and temperature rose to 102–104° F. Pain in left axilla. Crepitant râles throughout chest. Examination on Feb. 6. Temperature fell to normal on Jan. 29 but rose again suddenly on Feb. 2 and remained above 102° until death. Pulse and respiration changed in parallel way. Dulness over left lung passing into flatness over lower lobe. Tubular breathing with râles over lower lobe. Loud friction rub in left axilla. Right thorax resonant with coarse râles. Cyanosis and slight jaundice. Attempt at aspiration of left pleura resulted in withdrawal of bloody fluid from lung. This contained Pneumococcus Type IV. It was thought that bronchopneumonia followed the attack of measles with acute onset of lobar pneumonia on Feb. 3. Died Feb. 8, 8.30 a.m. Autopsy Feb. 8.

Anatomical Diagnosis: Clinical history of measles. Interstitial bronchopneumonia. Lobar pneumonia (left) with fibrinopurulent pleuritis.

Left pleural cavity.—Contains a considerable quantity of brownish green turbid fluid; the lung is bound by light fibrous adhesions to the diaphragm and pericardial sac. Posterior portion of upper lobe and whole lower lobe are covered with a thick fibrinous exudate and so also is the parietal pleura. *Right pleural cavity.*—There is no excess of fluid and the pleural surfaces are everywhere smooth and glistening. *Left lung (Fig. 53).*—The lobes are glued together by yellow fibrinous exudate. The upper lobe is collapsed but not consolidated. The interlobular septa are very distinct. The bronchi are thickened and grey with yellowish white opaque contents. The lower lobe is completely and uniformly consolidated; the cut surface is grey except for a small area in the center of the lobe which is hemorrhagic. The alveoli are filled with plugs of exudate which stand out above the cut surface giving it a rough granular appearance. The septa are not distinct. The bronchi are filled with a yellow exudate. *Right lung.*—The upper and middle lobes are cushiony, while the posterior portion of the lower lobe is blue and heavy.

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There are numerous minute hemorrhages in the pleura about the interlobar clefts. The whole lung is readily insufflated except a small part of the upper lobe. Through all the lobes there are found on section small greyish areas of consolidation about 2 to 3 mm. in diameter frequently surrounded by hemorrhage and containing a central bronchiole. One of these patches in the lower lobe is 1 cm. in diameter.

Microscopic Examination.—The left lung shows a typical lobar pneumonia with uniform densely packed exudate in the alveoli. The bronchi contain a purulent exudate. Their walls are slightly infiltrated with mononuclear cells. The alveolar walls are not thickened; the capillaries appear rather bloodless but contain a few megalocaryocytes. The exudate in the alveoli is almost entirely composed of leucocytes with very few red corpuscles. The leucocytes are ragged and in certain places reduced to fragments of nuclei. In these places the alveolar walls become indistinct and the capillaries appear to contain hyaline thrombi. There is little to suggest the features of the interstitial bronchopneumonia within the area of lobar consolidation.

Very few organisms can be found in the alveolar exudate but two or three were found in one alveolus. The right lung shows small bronchi filled with an exudate of leucocytes and with walls much thickened by the infiltration of these cells and mononuclear cells. The walls of the adjacent alveoli are thickened and infiltrated and they contain leucocytes and desquamated epithelial cells and much pigment. The occurrence of pigmented epithelium suggests the possibility of a local obstruction to the outflow of blood or a local chronic passive congestion. There is also a great deal of free blood in these alveoli. The bronchi contain streptococci in pairs and rather long chains.

Cultures from the blood and right lung showed *Streptococcus hæmolyticus*. Those from the left pleural fluid showed Pneumococcus Type IV and the streptococcus.

Case 50.—L. J. W., age 19 yrs. Never had measles. The patient was vaccinated against typhoid on Jan. 26, 1918, and had a severe reaction. He felt so badly that he was sent to the hospital where after about a week he developed measles, on Jan. 30. Rash lasted 2 days. Then he walked about the ward for a few days when he began to have a pain in his chest and shortness of breath. Coughed and expectorated a great deal and vomited. On Feb. 10 he was found to have a hacking cough but no difficulty in breathing. Did not seem very sick. Dulness over right upper lobe with harsh breath sound. Fine moist râles over both lower lobes behind. On Feb. 15 complained of bad stitch in left side; cough short and grunting. Marked dulness in lower left back with suppression of breath sounds. Feb. 16, 1918, 10 cc. of turbid fluid aspirated from left side. Feb. 18, operation for drainage of left side. Died Mar. 2, 1918. Sputum on Feb. 14 gave *B. influenzæ* and *Streptococcus hæmolyticus*. Blood culture on Feb. 14 negative. Pleural fluid Feb. 16 showed *Streptococcus hæmolyticus*. Autopsy Mar. 3, 1918.

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Anatomical Diagnosis: Lobar pneumonia with empyema (left). Interstitial bronchopneumonia (left).

Left pleural cavity.—In the left posterior axillary line there is a wound over the 9th rib from which protrudes a rubber drainage tube discharging a small amount of foul smelling fluid. The lung is bound on the anterior margin by light fibrinous adhesions which become more dense as the empyema cavity is approached. Between the anterior margin of the lung and the pericardium there is an encapsulated pocket containing 50 cc. of thick greenish yellow pus. The base of the lung is densely adherent to the diaphragm by fibrinous adhesions. The pleura over the anterior part of the lower lobe is covered with a thin fibrinous exudate, while that over the anterior portion of the upper lobe is smooth and glistening. The pleura over the posterior surfaces of the upper and lower lobes is covered by a thick fibrinopurulent exudate, the parietal pleura corresponding with this showing a similar exudate. The empyema cavity contains only a few cc. of pus. *Right pleural cavity.*—There is no excess of fluid, the lung is free from adhesions, and the pleural surfaces are everywhere smooth and glistening. *Left lung.*—Except for the anterior margin of the upper lobe the whole left lung is consolidated and on section both lobes are greyish red in color with a few scattered areas which are more hemorrhagic. There appears to be no thickening of the bronchial walls although the bronchi are filled with purulent material. The mucosa is hemorrhagic. The bronchial lymph glands are slightly enlarged. *Right lung.*—The whole lung is uniformly air-containing except for a slightly firmer patch in the upper lobe which on section is slightly more greyish than the surrounding lung but does not seem definitely consolidated; the alveoli contain no plugs of exudate which project above the surface. There is no thickening of the bronchial walls although they contain a thick creamy pus. *Pericardium.*—Contains 50 cc. of slightly turbid fluid with a few floating strands of fibrin. The surfaces are slightly injected with an occasional petechial hemorrhage but they have not lost their gloss.

Cultures from the pericardial fluid gave *Streptococcus hæmolyticus* in pure culture. Those from the lung, pleural pus, and blood gave also *Streptococcus hæmolyticus* but contaminated with a Gram-negative bacillus.

Microscopic Examination.—The left lung shows a pleura which is converted into a thick layer of granulation tissue surrounded by dense fibrin. The interlobular septa are not conspicuous. The bronchi are scarcely altered. The alveolar walls are of normal thickness, the alveoli filled with leucocytes. There is little evidence of blood or even of any considerable amount of fibrin. In many places the alveolar walls become scarcely visible and a whole area seems to fuse into a mass of leucocytes. In other places the leucocytes in each alveolus are reduced to a dust of fragments. Many Gram-positive cocci are present among the leucocytes in the exudate. These are in very short chains, although there are sometimes as many as ten in a chain. They are quite large and elongated and grow rather stiffly and not in sinuous lines. One has the impression that they may be

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pneumococci and not streptococci, although only the latter were cultivated from the lung and pleura. Their distribution and the nature of the lesion suggest this strongly. There are places in the same lung, however, beneath the thickened pleura but in areas not consolidated by the alveolar exudate in which the interlobular septa are thickened and contain thrombosed lymphatics. The alveoli contain fluid and desquamated epithelium and their walls are infiltrated with mononuclears. The bronchi are greatly thickened and infiltrated with mononuclears and show thrombosed lymphatics in their walls. In a word, the whole picture is that of interstitial bronchopneumonia.

The right lung seems normal. This may be a lobar pneumonia caused by the pneumococcus in which a secondary infection has overgrown the first.

Case 180.—W. H., age 27 yrs. Negro. Had German measles beginning on Apr. 28, 1918. No history of measles. Entered hospital May 7, when a diagnosis of lobar pneumonia involving the right lower lobe was made. Sputum was yellow, mucopurulent, and nummular, and was found to contain Pneumococcus Type II atypical, and influenza bacillus. Blood culture on May 8 gave a pure culture of Pneumococcus Type II atypical. There was acute pharyngitis. Died May 11, 1918, 2 a.m. Autopsy May 11, 1918, 10 a.m.

Anatomical Diagnosis: Clinical history of German measles. Lobar pneumonia (right upper and middle lobes). Interstitial bronchopneumonia (right middle and lower and left lower lobes). Serofibrinous pleurisy (right). Ulcerative laryngitis.

Left pleural cavity.—Contains no fluid. The surfaces are smooth and glistening. There are no adhesions although both costal and pulmonary pleura are extensively scarred. *Right pleural cavity.*—The surfaces are slightly glued together by a thin fresh fibrinous exudate which contains about 20 cc. of turbid brownish fluid. The surfaces are dulled over the whole lung. *Left lung.*—The lung is voluminous; the pleural surfaces are smooth. The upper lobe is cushiony and on section is air-containing throughout. In the lower lobe there are some firm patches in the posterior lower margin. Most of the lower lobe is air-containing, but there are some small patches of consolidation surrounded by zones of collapsed lung in the posterior portion. *Right lung (Fig. 54).*—The lung is very large and heavy, the upper and middle lobes except for the apical and anterior marginal portions being firmly consolidated. The lower lobe is largely collapsed and feels nodular throughout. On section the whole lower and posterior parts of the upper and middle lobes are consolidated and greyish red in color, each alveolus containing a plug of greyish exudate. The anterior portions are air-containing in general, but there are small patches of collapse and a number of small nodular peribronchial consolidations which can be traced to some extent into the area of lobar consolidation. In the lower lobe the tissue is air-containing and appears normal except in the lower posterior portion where there is a group of firm greyish nodules surrounded by collapsed lung tissue. The bronchi are reddened and contain a turbid frothy fluid. The bronchial glands are enlarged, soft, and grey. The mucosa of the trachea is deeply reddened. *Organs of the neck.*—The base

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of the tongue and the pharynx in general are reddened. The tonsils are much enlarged. There are ulcerations over the back of the uvula and on the sides of the nasopharynx behind the pillars of the fauces. The posterior aspect of the epiglottis is reddened but not ulcerated, but the vocal cords are rather deeply ulcerated on both sides. The mucosa of the larynx is red and there is a ragged dull opaque area on the right side below the vocal cords.

Cultures at autopsy showed *Streptococcus hæmolyticus* in the heart's blood, left lung, and right pleura. Pneumococcus Type II atypical was recovered in culture from both lungs. Gram-positive diplococci were found in smears from the larynx.

Microscopic Examination.—Section of the vocal cord shows a superficial loss of substance with an inflammatory reaction and numerous streptococci on the surface of the necrotic material. There are remnants of coagulated epithelium and many fragmented leucocytes in the surface layer. The ulceration is not very deep, but the streptococci are found in the crevices of the tissue for a considerable distance below the surface.

Sections from the upper lobe of the right lung show a rather thin but dense fibrinous exudate over the pleura. The surface of this is sprinkled with Gram-positive micrococci in pairs and short chains.

The interlobular septa are wide and edematous and infiltrated with fibrin. The lymphatics are very large and are filled with blood, leucocytes, and mononuclear cells and fibrin. Gram-positive cocci are abundant among these cells.

The bronchi are rather delicate and although their walls are slightly infiltrated with mononuclear cells they are not thickened. Their lymphatics are plugged in exactly the same way as those of the septa and blood vessel walls. The alveolar walls are normal in thickness. The cavities are filled with a uniform exudate of polymorphonuclear cells with occasional red corpuscles and a network of fibrin. There are many cocci in pairs evenly distributed and often contained in leucocytes. In the margins of the area of consolidation some of the bronchi are more definitely thickened and infiltrated, and the same condition is found in the walls of some blood vessels. The alveolar exudate remains the same. In the lower lobe the condition is different. The pleural changes are about the same, the interlobular septa wide with lymphatics obstructed by massive thrombi. But the bronchi even to their smallest branches are greatly thickened. They contain massed leucocytes with streptococci and numerous influenza bacilli. The epithelium is in some instances destroyed and gives place to a necrotic lining layer. The walls are like a loose vascular granulation tissue with radially placed blood vessels and dense mononuclear infiltration. The alveolar walls are enormously thickened. New connective tissue has formed in their thickness as in the bronchial walls and they are densely infiltrated. The alveolar cavities are filled with blood in many places especially near the bronchi, but others are filled with fluid. All contain desquamated epithelial cells, some mononuclear cells, and dense plugs of fibrin. In many cases there is evidence of or-

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ganization of the exudate, and columns of vascular granulation tissue extend into the bronchioles.

There is in this case a sharply defined lobar pneumonia in one part of the lung and an equally distinct and characteristic interstitial bronchopneumonia in other parts. From the one the pneumococcus was isolated, from the other the streptococcus. The lesions overlap scarcely at all. Influenza bacilli are scattered widely through the lung and are found in the larynx.

Several cases are separated to form this group because the lung shows a typical lobar pneumonia in one lobe and equally typical lesions of interstitial bronchopneumonia scattered through the remaining tissue of the same lung. This is especially striking in Cases 21 and 180 in which the pneumococcus was cultivated from the area of lobar pneumonia and the streptococcus from the bronchopneumonia lesions. Similarly these organisms could be demonstrated in as far as their morphology permits of their recognition, in characteristic distribution in the corresponding lesions. Influenza bacilli accompany the streptococcus in Case 180 but there are none in Case 21.

In several cases, Nos. 33, 36, and 45, in which there were definite lesions of lobar pneumonia in the lungs and in which the pneumococcus had been isolated from the blood during life or was isolated from other lesions at autopsy, it had been overgrown and killed by the streptococcus in the lungs without the development of typical streptococcal lesions there. In one case, No. 25, in which the pneumococcus was cultivated from the area of lobar pneumonia, it was nevertheless difficult to demonstrate many organisms in the sections. The lung was supposed to be in a state of resolution and it seemed probable that most of the organisms had disappeared. These examples tend to show that the pneumococcus is in many instances at least not a very persistent organism and may be supplanted by another such as the streptococcus. It is possible, although I think we have no strong evidence to prove it, that in the cases of the present series in which both organisms are present and alive with characteristic lesions produced by each in the lung, the pneumococcus in producing lobar pneumonia has acted as the forerunner and predisposing agent to infection with the streptococcus.

The lobar pneumonia in these cases is typical and within its area there are practically none of the interstitial changes which belong

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to the streptococcus. The pleura over it is thin and shows no granulation tissue formation; the bronchi are filled with exudate but otherwise are scarcely altered. One passes abruptly from this into the rest of the lung where typical interstitial bronchopneumonia prevails. Even the pleura seems to become slightly thickened and hyperemic, and the interstitial changes in the bronchi and framework of the lung stand out clearly. But it is difficult to trace these lesions into the area of lobar pneumonia. It is as though the two processes excluded each other, as though the lobar pneumonia once developed formed a barrier to the invasion of the streptococcus but more especially to its power of stirring the tissues to a special type of reaction. One might say that having completed one maneuver of defense the tissues are unable to carry out a different one at once.

On the whole, one is impressed with the probability that the pneumococcus was the first invader. Whether the pneumococcus could gain a foothold in a lung already the seat of extensive lesions caused by the streptococcus seems questionable.

The following somewhat imperfectly studied case is introduced at this point because it seems important in suggesting the possibility that the combination of lobar pneumonia and interstitial bronchopneumonia may be brought about by the pneumococcus alone. In this instance culture from the sputum made 11 days before death showed the predominance of Pneumococcus Type II, and blood culture made on the same day showed the same type of pneumococcus. Unfortunately no cultures were made at autopsy and *Streptococcus hæmolyticus* was never demonstrated. Even in the tissues the organisms resemble morphologically the pneumococcus rather than the streptococcus. Influenza bacilli are not present in the sections. Nevertheless there are not only extensive lesions of the type of lobar pneumonia but also characteristic interstitial bronchopneumonic lesions. Since the latter changes have been shown to occur in cases of pure infection with *Bacillus influenzæ*, there is no reason to suppose that they could not be produced by the pneumococcus, but if this is accepted as the interpretation of the case, it stands alone in our material.

Case 196.—R. G., age 25 yrs. Admitted May 5. Died May 18, 1918. Onset about May 1 was gradual with slight pain in the chest, cough, and aching

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in back and legs. Physical examination on admission revealed dulness over the right lower lobe, with fine râles, and high pitched expiration. On May 8 there was dulness with distant bronchial breathing over the right upper lobe. May 10, delirium. May 11, dulness and bronchial breathing over the left lower lobe. Voice sounds somewhat diminished as though by fluid. Cyanosis. Temperature high in the beginning, 103–105°F.; later 101–103°. During the last 4 days about 104°. Leucocytes 12,000–20,000. Sputum culture on May 7 showed as the predominant organism Pneumococcus Type II. Blood culture on May 7 showed Pneumococcus Type II in considerable numbers. Autopsy May 18, 4 hours after death, by Major Glomset.

Anatomical Diagnosis: Lobar pneumonia (left upper lobe). Bilateral interstitial bronchopneumonia. Acute splenic tumor.

Left pleural cavity.—There is no accumulation of fluid. The surfaces are glued together by fibrin over the upper lobe of the lung but are easily separated. *Right pleural cavity.*—No excess of fluid is present. The surfaces of the lower part of the upper lobe and the middle lobe are covered with fresh fibrinous exudate. *Pericardial cavity.*—Contains 100 cc. of clear straw-colored fluid. The surfaces are smooth. *Left lung.*—The lung is not collapsed. In the upper lobe there is a patch of coarsely granular consolidation which is greyish in color and involves the upper half of the lobe. The lower lobe is studded with small greyish nodules which are related to the bronchioles and surrounded by dark brown peripheral zones. *Right lung.*—The upper lobe contains a number of palpable nodules which on section are branched, grey or greyish yellow, and often surrounded by hemorrhage. There are in the anterior part two distinct areas of consolidation which are granular with hemorrhagic patches. In the lower lobe there are numerous small nodular areas of opaque yellowish grey. These branch and follow the bronchioles and several are seen within a single lobule (Fig. 55).

Microscopic Examination.—The area in the left upper lobe shows the alveoli filled with an exudate of leucocytes among which abundant pneumococci are found. In the lower lobe and elsewhere throughout the lung the lesions are typically those described as interstitial bronchopneumonia.

The pleura is practically unaltered. The interlobular septa are widened with some infiltration of cells but especially by the greatly dilated and thrombosed lymphatics which can be traced into the arterial and bronchial walls. The bronchi are filled with masses of leucocytes among which are Gram-positive diplococci, often separated by a space from the adjacent material and therefore appearing to have a capsule. These are sometimes in short chains of four or six but never in long sinuous chains. Influenza bacilli were carefully searched for, but were not found. The mucosa of the bronchi is greatly swollen and the wall thickened by the formation of a loose, very vascular granulation tissue with abundant mononuclear wandering cells. The adjacent alveoli are filled with dense plugs of fibrin with many red corpuscles and some desquamated epithelial

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cells. The fibrin is in many places partly or completely organized and clothed in a single layer of epithelium. Hemorrhage of a fresh character is, however, prominent. The alveolar walls and indeed all the tissues of the lung about the infected bronchi are thickened and infiltrated with mononuclear cells.

In connection with these peribronchial changes there are numerous small patches of consolidated lung tissue in which the alveoli are packed with leucocytes together with phagocytic epithelial cells. In these areas the cocci are scattered in great abundance, although elsewhere they are practically confined to the bronchial contents and lymphatics.

6. Old Empyema.

Case 52.—H. C., age 24 yrs. Entered the hospital Jan. 12, 1918, with fever of sudden onset beginning 3 hours before he was brought to the hospital. Breathing was rapid and he was expectorating a reddish foamy sputum. Dulness over right lower chest behind and breath sounds scarcely audible. On Jan. 15 the breath sounds became tubular over this area, but on Jan. 26 they were again inaudible, although the dulness persisted. Pus was aspirated from the chest and found to contain pneumococci. On Jan. 28 the 8th rib was resected and the thorax drained. The temperature which was irregular and ranged up to 104° F. fell and remained normal until about the middle of February when it again became irregularly elevated. On Feb. 22 the 7th rib on the right side was resected. Smears from the pus discharged showed a Gram-positive diplococcus, but no culture was made. After the second operation the patient's temperature became practically normal and he seemed to be doing well. He died suddenly upon sitting up in bed on Mar. 4. Autopsy Mar. 5, 1918.

Anatomical Diagnosis: Empyema (right) with drainage. Atelectasis of right lung. Embolism of pulmonary artery.

Left pleural cavity.—Contains no excess of fluid; surfaces are smooth and glistening. *Right pleural cavity.*—There is a small partly healed wound in the right axillary line over the 8th rib. In the right midscapular line there is a fresher wound from which blood and pus exude through a rubber tube. On opening the thorax it is found that the mediastinal tissues on the right side are infiltrated with a purulent exudate. There are dense adhesions between the base of the lung and the diaphragm and with the costal pleura over the whole lower and anterior part of the lung. From the apex downward and extending half-way forward there is an unobliterated part of the pleural cavity which is lined with thick red velvety granulation tissue and filled with purulent fluid. It is found that the old operation wound extends through the 8th rib, a part of which has been removed. This wound is incompletely healed internally. The second operation wound involves the same rib with removal of another portion. *Left lung.*—Normal throughout, but in the pulmonary artery there is impacted a folded mass of thrombi which are loose but large enough to

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occlude it. These thrombi are nowhere adherent and the wall of the blood vessel is normal. *Right lung.*—The pleura on the upper posterior aspect is covered with granulation tissue as described. The bronchi are slightly reddened. On section the lower lobe posteriorly is completely collapsed, but there is no area of consolidation. The upper and middle lobes are air-containing throughout. The pulmonary artery contains several large thrombus masses one of which is bent upon itself and glued together in that position by a fresh clot. Another is smaller and hollowed out. They are sufficient to occlude the artery, the wall of which is smooth except for one small patch which is slightly roughened.

The iliac veins are normal on both sides and the walls perfectly smooth. The femoral veins are smooth as far as they could be opened and nothing but liquid blood could be pressed up from them. The pelvic veins show no thrombi. The vena cava is smooth throughout. So too the azygos, the jugulars, subclavians, and other veins seem quite smooth and contain no thrombi. The heart is not enlarged and rather flabby and soft. The endocardium is smooth throughout; the valves are delicate and competent. There are no thrombi.

Smears from the lung tissue and pleural fluid showed many Gram-positive diplococci often in short chains, but in cultures these were overgrown by a Gram-negative bacillus with putrefactive odor.

Microscopic Examination.—The right lung shows in part a thick fibrous pleural covering. Where it adjoins the empyema cavity and in the interlobar adhesions there is a vascular granulation tissue filled with mononuclear and plasma cells. There are certain round empty spaces surrounded by giant cells, evidently produced by some foreign body. The lung itself is extensively collapsed and the alveoli are filled with pigmented epithelial cells. This represents a local chronic passive congestion caused by the collapse. Otherwise no especial alteration of the lung substance is to be observed. The left lung is normal. The thrombi in the pulmonary artery show the characteristic architecture with strands of platelets bordered by leucocytes. They are fresh and show no signs of organization.

Case 53.—R. J. O'M., age 23 yrs. History negative. On Feb. 1, 1918, he had a severe chill followed by high fever and a pain in his right side and was admitted to the hospital. Physical examination at this time was negative although the temperature was 102.4° F. and the pain in the side distressing. On Feb. 6 leucocytes were 23,000 (polymorphonuclears 94 per cent). There was some abdominal pain and rigidity. Temperature ranged from 101–104.6° F., respiration 20–40. On Feb. 12, 150 cc. of pus were aspirated from the left chest and a streptococcus was found in smears and cultures. On Feb. 14 the 7th rib was resected under local anesthesia. Temperature remained as before and patient died on Mar. 5, 1918. Autopsy Mar. 6, 1918.

Anatomical Diagnosis: Multiple pulmonary abscesses. Bilateral empyema.

Left pleural cavity.—Partly obliterated by fibrinous adhesions in the upper portion, while in the lower part the lung is retracted from the chest wall and the pleural surfaces are covered with a thick fibrinopurulent exudate. In the axillary

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line over the 11th rib there is an incision wound and a portion of the rib has been removed. Very little fluid remains in the cavity. *Right pleural cavity.*—Partly obliterated by adhesions, but in the lower portion there are about 300 cc. of purulent fluid. The lower lobe of the lung is collapsed and the pleural surfaces are covered by a yellow fibrinopurulent exudate. The anterior border of the lung is adherent to the pericardium and beneath it is an encapsulated pocket containing about 50 cc. of turbid fluid. *Left lung.*—The lower lobe is collapsed, but the whole lung can be inflated artificially except the posterior inferior portion of the upper lobe. The upper lobe is air-containing on section except for an area 7 cm. in diameter in the posterior part, which is greyish red and consolidated. It includes several soft yellow areas which project above the cut surface. In the lower lobe there are several yellow areas which are irregular in outline and frequently confluent and surrounded by consolidated lung. These are fairly firm and contrast sharply with others which measure about 0.5 to 1 cm. and are slightly elevated. The latter are filled in the center with a dark greyish fluid which can be readily expressed, leaving a crater-like depression with necrotic sides. They are not surrounded by so much induration as the firmer yellow areas. Bronchial glands are enlarged and softened but contain no foci of caseation. *Right lung.*—The pleura is slightly thickened and covered with a ribbed fibrinous exudate. In the upper lobe the texture is coarse, and the septa are prominent. There is a yellowish grey flecked consolidation in the lower part of the upper lobe and in the middle lobe. This is not uniform but appears to form a sort of network of alternating spongy and grey translucent tissue often mottled with yellow. There are several abscesses measuring 3 to 5 mm. or even more and surrounded by a halo of red. The lower lobe is air-containing but has one abscess about 1 cm. in diameter in its upper portion. The lymph glands are enlarged and soft.

Cultures at autopsy gave the hemolytic streptococcus in blood and pleural and pericardial fluid, but in each case it was overgrown by a Gram-positive bacillus.

Microscopic Examination.—The pleura over the left lung is covered with thick granulation tissue and fibrin. In places the interlobular septa are thickened and contain lymphatics filled with bacteria and leucocytes. In certain areas the lung substance is not much altered except that throughout sharply outlined patches which reach up to the pleura the alveoli are filled with a purulent exudate with abundant bacteria. The neighboring alveoli are flattened and collapsed. In the central portion the bacteria form a cloud and the cells including the walls of the alveoli have become necrotic. In other areas there are no abscesses but there is an advanced organization of exudate in the alveoli. The strands of new connective tissue are covered with epithelial cells. In the center of some of these strands there are spaces lined with epithelium which look almost as though it were attempted to produce new alveoli there.

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Case 57.—H. H. H., age 18 yrs. History negative. On Jan. 18, 1918, the patient had a cold followed by weakness and anorexia. Since Jan. 27 has felt worse and there has been pain in the right chest. On Feb. 1 had a definite chill and was admitted to the hospital. Physical examination was negative except for signs of fluid in the right pleural cavity. Temperature 101° F., pulse 98, respiration 23. Leucocytes 23,400. On Feb. 3, 30 cc. of cloudy fluid were aspirated from the right chest, and streptococci were found in smears and culture. This was repeated on Feb. 8, and on Feb. 13 the 7th right rib was resected and drainage established. On Feb. 18 the temperature rose to 102.4° and continued to range between 100° and 104° until death on Mar. 8, 1918. Autopsy Mar. 8, 1918, at 1.30 p.m.

Anatomical Diagnosis: Empyema (right side) with drainage. Atelectasis of right lung. Subacute pericarditis.

Pericardial cavity.—Contains a small amount of fibrinopurulent exudate. The parietal and visceral layers of the pericardium are granular and covered with fibrin and in a few places are bound together by frail adhesions. The surfaces are flecked with hemorrhages. *Left pleural cavity.*—Contains no fluid; the surfaces are smooth and glistening. *Right pleural cavity.*—In the right axillary line there is a wound 10 by 5 cm. with necrotic edges. This extends into the posterior part of the pleural cavity which contains about 400 cc. of dark greenish foul smelling pus. The pleural surfaces are covered with a greenish fibrinopurulent exudate about 5 mm. in thickness. The surfaces are bound together along the anterior margin of the lung. *Left lung.*—The lung is crepitant throughout and is everywhere easily inflated. On section there is no consolidation and the lung is normal in texture. *Right lung.*—The lung is collapsed against the vertebral column and is heavy and airless. There is no consolidation and the bronchi do not seem to be thickened but lumina are somewhat dilated. The bronchial mucosa is pale grey. Bronchial glands slightly enlarged and soft.

Cultures are not recorded from this case.

Microscopic Examination.—The left lung appears to be normal. The right lung is covered with a dense flattened fibrous granulation tissue over which is a thick layer of purulent material. The interlobular septa are very wide and dense like hard old connective tissue. The lymphatics where they are discoverable are embedded in this dense tissue, not enlarged but filled with leucocytes and mononuclear cells.

The bronchi are rather thick walled but have a scarred look as though they had receded from a previous thicker state. They are not densely infiltrated but are commonly full of leucocytes and other cells. The alveolar walls are very thick and are not only infiltrated with mononuclears but show an actual connective tissue thickening. They are usually empty and quite collapsed.

Case 165.—E. B. deL., age 22 yrs. On Apr. 18, 1918, developed German measles which was succeeded on Apr. 24 by mumps. Present illness began

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Apr. 27 with a pain in the right chest. Next day the diagnosis of lobar pneumonia with consolidation of the right lower lobe was made and confirmed by radiogram. Empyema developed Apr. 30, and was recognized by aspiration of fluid which contained *Streptococcus hæmolyticus*. Died May 4, 1918, at 5.35 a.m. Autopsy May 4, 1918, 5 hours after death.

Anatomical Diagnosis: Old interstitial bronchopneumonia with empyema (right). Acute fibrinopurulent peritonitis. Phlegmonous laryngitis.

Left pleural cavity.—Contains very little fluid. The surfaces are smooth anteriorly but posteriorly are dark blue and covered with hemorrhagic areas and fibrinous exudate. *Right pleural cavity.*—Contains about a liter of turbid fluid which is of the color of pea soup. There are a few floating shreds of fibrin. The right lung is flattened against the outside of the pericardium and is slightly adherent. The surfaces of the pleura are nodular and roughened and covered, except over patches where the lung has adhered, with yellowish exudate. Between the middle and lower lobes there are two pockets filled with yellow fibrinopurulent material. *Left lung.*—The lung is voluminous but the lower lobe is somewhat collapsed. On section the upper lobe is dry, coarse in texture, rather pale red, and everywhere air-containing. The anterior and upper parts of the lower lobe are quite similar, but the lower and posterior parts are dark red and collapsed with some projecting nodules which have pale grey centers. The bronchi in this lobe are deeply congested. Bronchial glands moderately enlarged. *Right lung.*—Small, pasty, and airless. On section it is almost entirely collapsed, but there is no consolidation except for a few fairly firm projecting nodules in the lowermost part of the lower lobe. *Larynx.*—The epiglottis and aryepiglottic folds are greatly swollen and vary in color from greyish red to opaque yellow. On incision the swollen tissues are found to be infiltrated with a purulent fluid. There are slight superficial ulcerations at the brim of the larynx, but the vocal cords are not altered. The trachea is slightly reddened. There are opaque yellow patches on the wall of the pharynx laterally. Tonsils reddened but not swollen. *Other organs.*—The peritoneum contains a yellow fibrinous exudate which glues together the intestinal loops and is especially abundant over the right lobe of the liver. There are two needle puncture wounds in the right axillary line on a level with the nipple. There are one or two points of hemorrhage in the diaphragm and there is a small opaque yellow point in the liver surrounded by a hemorrhagic area corresponding fairly well in position with the points of hemorrhage in the diaphragm.

Microscopic Examination.—The right lung shows a thick layer of granulation tissue replacing the pleura and covered with fibrin. The lung is completely collapsed but it can be seen that the bronchi and blood vessel walls are moderately infiltrated with mononuclear cells. The alveolar walls are thickened by a cellular infiltration and their cavities filled in part with fibrin and desquamated epithelium. Streptococci are seen in the bronchi associated with large numbers of Gram-positive spore-bearing bacilli.

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Section of the arytenoepiglottic fold of the larynx shows superficial ulceration. There is the most intense phlegmonous inflammation of the underlying tissue, part of which is spread wide by the accumulation of fluid, fibrin, and cells. But all this area of edema is necrotic and is found to contain myriads of streptococci which form a dense feltwork in the tissue.

No cultures were recorded.

Case 183.—H. P., age 24 yrs. Began May 2, 1918, with sore throat. Later there was pain in the chest beginning about May 5, and on May 7 the physical signs indicated a lobar consolidation of the right lower lobe. There was dulness to flatness over the right base with bronchophony and bronchial breathing. This was confirmed by the radiogram and the suggestion was made that there might be fluid in that pleural cavity. This was made certain by aspiration on May 10, and on May 12 a bloody fluid was aspirated from the pericardial cavity. The latter fluid gave on culture a mixture of *Streptococcus hæmolyticus* and influenza bacillus. The pleural fluid also gave the same combination. Blood culture made on May 7 was negative. Sputum on that day was tenacious and mucoid with no blood and contained both the hemolytic streptococcus and influenza bacillus. Died May 11, 1918, at 4.30 a.m. Autopsy May 11, 12 hours after death.

Anatomical Diagnosis: Slight pulmonary changes. Bilateral empyema. Acute fibrinopurulent pericarditis.

Left pleural cavity.—Contains about 150 cc. of yellowish turbid fluid. The surfaces are dull and the lung is slightly adherent to the pericardial sac and to the diaphragm. The tissues of the anterior mediastinum are thickened by an accumulation of turbid fluid. *Right pleural cavity.*—Contains 1,400 cc. of turbid fluid with much brown sediment which can be stirred up easily. It has the appearance of thin pea soup. The surface of the pleura is deeply reddened and is covered with a layer of yellow fibrin which is easily removed. There is a thick layer of fibrin between the lung and the right side of the pericardial sac. *Pericardium.*—The pericardial sac is enormously thickened and contains about 300 cc. of turbid yellowish fluid. The surface is covered with fibrin which overlies a translucent reddish granulation tissue in which there are some hemorrhages. *Left lung.*—The lung is heavy and blue, and although the upper lobe is largely air-containing the lower lobe is collapsed and in the posterior portion dark bluish red and pasty. There are patches of hemorrhage under the pleura between the lobes. On section no areas of consolidation are to be found. *Right lung.*—The lung feels flabby and is airless. No areas of consolidation can be felt and upon artificial inflation the whole is distended. On section there are no solid portions except for a small encapsulated tubercle at the apex. The bronchial glands are enlarged and purplish in color and those at the bifurcation of the trachea contain a few caseous tubercles. The tracheal mucosa is deeply reddened.

Cultures at autopsy showed the hemolytic streptococcus in the heart's blood, both lungs, right pleura, pericardium, and mediastinum. The influenza bacillus was found in cultures from the right pleura and pericardium.

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Microscopic Examination.—The pericardial surfaces are covered with an exudate of fibrin, but there is no underlying granulation tissue. The epicardium is edematous and infiltrated with cells, but the lining pericardial cells are still visible in most places. The superficial layer of the heart muscle is spread apart by an infiltration of leucocytes and mononuclear cells. The mediastinal fat bordering the pleura is edematous and infiltrated with leucocytes. In places the tissue has disappeared and given place to a mass of disintegrated leucocytes. Here streptococci in chains are found in enormous numbers. So too in the cellular debris which adheres to the surface of the fibrin on the pleural side, but no organisms are found in the denser fibrin or in the tissue where it has not undergone necrosis.

The right lung shows several caseous tubercles in one area and around them the connective tissue structures are dense and thickened. Throughout the rest of the lung, however, there is no definite alteration of interlobular septa, bronchi, or alveoli, except near the surface where there are patches of edema and hemorrhage with desquamation of the alveolar epithelium and fibrinous exudate in the alveoli; even here the bronchi are little changed. The pleura is converted into a thick layer of granulation tissue with overlying fibrin.

In the left lung over which the pleura is scarcely thickened it is similarly difficult to find any definite lesion in the lung. There are, however, patches beneath the pleura in which the alveoli are filled with partially organized exudate which is ensheathed in a layer of epithelium.

This case is one which would offer the greatest support to those who favor the idea of a primary pleurisy. The duration was only 9 days in all and only 6 days after the first pain in the chest was felt.

The question as to the mode of infection of the pleura has been discussed above and the cases of this group are detailed as examples in which it is difficult to determine the mechanism of infection. There are some who argue for the primary and independent infection of the pleura since they find cases such as these in which it is not easy to observe striking changes in the lungs other than the collapse which is caused by pressure. They must then have recourse to the idea that the bacteria are brought to the pleura by the blood stream because there is scarcely any other way in which the pleura could be infected. Since we have so regularly found cultures of the circulating blood sterile, this explanation does not seem acceptable.

It seems, on the contrary, necessary to hold to the idea that infection takes place by way of the trachea and bronchi and extends thence by way of the lymphatics of the lung (especially after they are obstructed by thrombi) to the pleura. The difficulty in explaining this origin of the pleurisy in such cases as have just been given is probably

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due to the fact that they are old cases in which the empyema has persisted for a long time during which it is conceivable that the pulmonary changes might have been healed. In Case 52 especially, the man was convalescent except for remains of his empyema, but died of pulmonary embolism. In Case 53 abscesses are present but there are remains of an old pneumonia which show as organized exudate, in Case 57 great thickening of the interlobular septa and alveolar walls, in Case 165 even recognizable remains of a diffuse interstitial bronchopneumonia. Even in Case 183, which was of only 9 days duration and in which the explanation of the pleurisy is especially difficult, there are slight changes in the lungs. But in all the others the tracing of the development of the lesions in the lungs which at first are not accompanied by pleurisy, into their later stages in which the lymphatics become so strikingly involved and pleurisy arises, seems to show clearly the dependence of the pleurisy upon intrapulmonary lesions.

7. Empyema.

The tabulation and analysis of 53 cases of all the types of pneumonia as they occurred shows an extraordinary frequency of pleurisy with fibrinopurulent effusion which is especially due to the activity of the hemolytic streptococcus. The term empyema which is in common use is not sharply limited in its significance, for although it should mean the filling up of the pleural cavity with pus it has been made to do duty in this epidemic for all those forms of pleurisy with extensive effusion in which although the exudate becomes distinctly purulent if the patient survives long enough, it is frequently in the earlier stages a thin watery brownish turbid fluid with a granular sediment and floating shreds of fibrin.

The profusion of this fluid exudate is shown crudely by the statement that although in thirteen of these cases the chest had been evacuated by resection of a rib and drainage, more than 28 liters of fluid were measured out at the autopsies.

In only seven of these cases was a fluid exudate in any considerable quantity found on both sides, and then usually there was a rather small amount only on the less affected side. At the autopsies fluid was found in quantities varying from 10 to 4,000 cc., but it is possible that

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this does not represent the extremes. 1,000 to 1,500 cc. were commonly found.

In the most acute cases in which the streptococcus has produced either peribronchial or lobular lesions in the lungs, the pleura is generally empty and its surfaces are smooth and glistening. This was true in practically all those in which death occurred within 8 days of the onset of the disease and also when fresh lesions developed in the lung opposite to that in which an old affection was found. But when the lung had been infected for 10 days or 2 weeks or more, the pleura nearly always contained an exudate. Then the surface was covered with fibrin overlying petechial hemorrhages, either as a rough thin layer or a thicker shaggy or ribbed coat of yellow or yellowish green.

The character of the fluid in these earlier cases is so distinctive that at the risk of repetition it should be described once more. Numerous epithets have been applied to it—it is like thin pea soup, like turbid urine, like unstrained bouillon, like muddy water, but generally like thin pea soup. It has often a greenish cast and the granular sediment which can be stirred up in a cloud tends to settle in the bottom of the pleura. Strands or flakes of fibrin float up in this or hang from the wall.

Later it rapidly becomes more turbid and thick and assumes a more purulent character, and especially when it is confined in localized areas by adhesions it is often thick whitish green pus. When the pleural cavity has been laid open by resection of the rib the fluid changes somewhat, and if it is secondarily infected with putrefactive organisms it becomes very foul and often blackish green.

It is most characteristic of the streptococcal pleurisy that organization of the fibrinous exudate occurs with great rapidity, causing the pleural membrane to become greatly thickened and converted finally into a thick red velvety granulation tissue from which the dense overlying fibrin can often be brushed off. This is so regular an occurrence that it is noted in 32 of the 42 cases of streptococcal pneumonia analyzed here, whereas it was observed in only one of the seven cases caused by the pneumococcus and then to a slight degree only. It is not meant that the organization of exudate and the consequent thickening of the pleural membrane is necessarily rare in other forms

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of infection, but the rapidity and regularity with which this occurs in the streptococcal infection are striking. The formation of adhesions between the lung and the surrounding tissues is of interest to the surgeon. In many cases there were no adhesions when a great quantity of fluid exudate had accumulated and then the lung was found collapsed and retracted and flattened against the mediastinal tissues or occasionally, receiving still a little air, floating on the fluid. The extreme collapse of the lungs and their consequent reduction to a blue pasty mass in which firm nodules were palpable was another striking feature of these cases.

In many instances there were adhesions which limited the displacement of the lung by the fluid or limited the distribution of the fluid. Many of these seemed to be old adhesions which antedated the present disease, others appeared to have been formed in the early days of the disease as a gluing of the surfaces with fibrin, and others still were found in later stages forming a limiting wall about the more or less localized empyema cavity. Occasionally adhesions were obviously due to the presence of an intrapulmonary abscess or other lesion which reached the pleura. In one or two cases such necrotic patches of the pulmonary pleura were well protected by the formation of adhesions.

The topography of adhesions in connection with well developed empyema is of especial interest. Occasionally what seemed to be old adhesions over the whole upper lobe maintained the position of that lobe, while the lower lobe was forced upward by the fluid collected below. In other cases dense adhesions between parts of the lobe or parts of the pulmonary and costal surfaces left communicating channels connecting with the main cavity.

Encapsulated pockets of pus are sometimes found and in this series there were thirteen examples of this. In nine cases the pus was imprisoned between the mesial surface of the lung and the outside of the pericardial sac by adhesions between the anterior margin of the lung and the mediastinum, between the base of the lung and the diaphragm, and between the posterior margin of the lung and the posterior mediastinal tissues. Sometimes as much as 300 cc. of pus were thus enclosed. Of the nine cases three also showed pockets of pus in the adhesions between the lobes of the lung and there were

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three others in which this occurred alone. In two cases there was found a collection of 100 cc. of green pus between the base of the lung and the diaphragm, and in one or two there were small collections walled off between the lung and chest wall. While many cases showed encapsulation of exudate at autopsy, it is possible that such pockets were broken in some of the thirteen cases in which the pleura had been opened by the surgeon, although in three of the cases in which pockets of pus were found in these situations at autopsy there had been resection of a rib and drainage. On the whole this is not a large proportion, but the failure to discover such pockets is a constant source of anxiety to the surgeon.

There were eleven cases of lobar pneumonia caused by the pneumococcus, among which two were also infected with the streptococcus and showed large purulent pleural exudates. The others had little or no fluid exudate, but the pleural surfaces were glued together by fibrin. There was no organization of the fibrin nor any thickening of the pleural membrane by granulation tissue.

This stands in sharp contrast to the condition in the streptococcal cases. Indeed in those instances, such as Case 21, in which there were both pneumococcal lobar pneumonia and interstitial bronchopneumonia in the same lung, the pleura was thickened over the lobe affected by the streptococci but thin over that lobe occupied by the lobar consolidation.

There was one case, No. 188, of lobar pneumonia with organization of the exudate over which the pleura was slightly thickened, but another case, No. 45, of long standing in which both pleural cavities were obliterated by fresh fibrous adhesions. In both these cases the lungs contained abundant influenza bacilli. In most of the cases of lobar pneumonia death occurred while the pleura was covered with unchanged fibrin.

The impression seems to prevail that abscess-like accumulations of pus in the mediastinal tissues are common in the cases of streptococcal empyema. I think, however, that it is usually the pocket of pus between the mesial surface of the lung and the mediastinal tissues which is mistaken for a mediastinal abscess. Nevertheless there was in Case 183 a moderate accumulation of turbid purulent fluid in the tissue of the anterior mediastinum below the level of the remnant of the thymus, and a similar infiltration was observed in Case 52.

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8. Epidemiological Relations.

The relation of measles to severe and fatal pulmonary inflammations has always been recognized. So too the importance of measles as a predisposing disease in epidemics of pneumonia has been fairly accurately appraised since early times and is definitely mentioned by the writers who describe the pandemic of 1812.

It is not known, however, in just what way measles facilitates the invasion of the streptococcus. Very little is known of the actual changes produced by measles in the respiratory tract. In all the great epidemics of measles death appears to have depended largely upon pulmonary infection or else upon the fatal effects of exposure, starvation, and lack of care that accompanied several of the outbreaks among savage people.

Such autopsies as have been performed upon cases of supposedly uncomplicated measles have left us with only very vague results, and we are in no better position to estimate the part played by measles in the production of the fatal lesions than were those who described the epidemic during the War of 1812, except that we know that in our experience the anatomical changes in the bronchi and lungs are always associated with the presence of *Streptococcus hæmolyticus*. We know further that this streptococcus can cause the same changes without any predisposing measles and that they are produced in practically identical form in children after whooping cough and diphtheria and, from at least one case in an adult, after scarlet fever. We are therefore inclined to ascribe none of the actual anatomical changes which we can see to measles, but all to the secondary invader.

Nevertheless it is certain that measles plays an important part. In the Texas autopsy material, if we exclude 7 cases of uncomplicated lobar pneumonia due to the pneumococcus, there were 28 cases of streptococcal pneumonic infection, and of these 15 had recently had measles or were still covered with the rash. At Camp Dodge, Iowa, of 23 cases of streptococcal pneumonia, 8 had just passed through measles and 3 had had German measles. In this epidemic, however, these particular figures are misleading since they depend upon a fresh outbreak of measles pneumonia at the end of a long epidemic in which measles had played no considerable part, the few cases of measles having been thoroughly isolated in a distant barrack.

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This accidental and sudden flare up of streptococcal bronchopneumonia in a barrack of measles patients among whom there had previously been no pneumonia, although a great epidemic was prevailing in the general camp, brings out two important points. First, that in this camp the streptococcus had gained a foothold independently of measles and produced an extensive and fatal epidemic of interstitial bronchopneumonia. Second, that when this infection did attack patients ill with measles the bronchopneumonia was much more severe and more quickly fatal. It was among these cases that we found the freshest lesions in patients who had died 4 to 8 days after the beginning of the bronchial symptoms. It was almost exclusively among these patients too that we observed the hoarseness and loss of voice which was explained by finding deep ulcerations of the vocal cords and laryngeal walls.

Therefore it seems justifiable to conclude that measles brings about a most effective predisposition to infection with the hemolytic streptococcus, although the streptococcus can invade and even cause great epidemics without its aid. In addition it may be emphasized that the combination of streptococcus infection with measles seems to produce a far more intense affection than the streptococcus alone, but in this we cannot yet recognize any anatomical changes that are due to measles itself.

At this point it may be said that these epidemics of streptococcal bronchopneumonia have not been confined to troops in camp but have existed in a more moderate form in the civilian population at many points. Among children the production of typical interstitial bronchopneumonia after measles and whooping cough has been recognized at autopsy in a number of cases.

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SUMMARY.

During the winter and spring of 1917–18 there has prevailed a great epidemic of measles among the troops quartered in the army camps. It has been especially prevalent in the southern camps. This is probably partly due to the fact that the recruits in the South are largely from remote rural districts and are therefore more susceptible than those in northern camps where the proportion of city dwellers is larger and the intercourse of rural dwellers more extensive.

Associated with this epidemic in the southern camps there has been a great epidemic of a peculiar form of pneumonia caused by a hemolytic streptococcus.

Although this was found to follow measles in a great proportion of cases it also affected men who were recovering from some other disease such as scarlet fever and frequently spread among those who had suffered no predisposing disease. In at least one northern camp in which we worked there had been no significant outbreak of measles, but an independent epidemic of streptococcal pneumonia arose and caused great ravages. Toward its conclusion some patients with measles who were isolated in a distant barrack became infected and died rapidly with a most intense and acute form of the disease.

Lobar pneumonia caused by the several types of pneumococcus occurred throughout these epidemics, but the number of cases seemed not especially different from what ordinarily occurs during those months of the year. In some cases lobar pneumonia was combined with streptococcal pneumonia. Otherwise there was nothing peculiar about the pneumococcal infections.

The streptococcal infection seems to occur by way of the upper respiratory tract and the illness commonly begins with a sore throat, fever, and cough. The physical signs in the lungs are often indefinite until evidence of accumulation of fluid in the chest appears. Dyspnea of the most extreme type especially during inspiration is characteristic and results in a livid cyanosis. Many of the patients become hoarse or lose their voices entirely. They are alert, apprehensive, and sleepless, and there is often delirium.

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Two main types of pulmonary lesions have been described, although these are frequently combined.

The first, designated interstitial bronchopneumonia, is essentially the result of infection of the bronchioles with large numbers of hemolytic streptococci which leads to great changes in their walls and in the adjacent pulmonary tissue.

The most striking accompaniment of this is a patchy atelectasis or collapse of the lung affecting those portions formerly supplied with air by the obstructed bronchi together with the formation of firm nodules of consolidation about the terminal portions of the bronchi. In addition to this there is extreme engorgement of the blood vessels of the lung and hemorrhage into its tissue about the nodules of consolidation.

The walls of the bronchi themselves become densely infiltrated with mononuclear cells and thickened. Extreme hyperemia and the new formation of blood vessels and of connective tissue add greatly to this thickening and to the deformity of the wall. In some cases the whole lining becomes necrotic and coagulated and constitutes a diphtheritic pseudomembrane. Corresponding with the changes in the bronchial wall are those in the walls of the adjacent alveoli which become greatly infiltrated with mononuclear cells, the alveolar capillaries are distended with blood, the epithelium is proliferated rapidly and desquamated into the alveolar cavity. These cavities are found to be filled in the neighborhood of the bronchus with blood, dense fibrin, a few mononuclear cells, and greater numbers of desquamated epithelial cells. Those which are more distant contain diminishing numbers of these cells but are filled with a thick viscid fluid. This rather gelatinous edema gives a semblance of confluence between these areas of consolidation before it is really completed. But there are many cases in which the changes are restricted to the neighborhood of the bronchioles and separated from each other by wide areas of normal air-containing tissue. Streptococci may be found in tangled masses in the lumen of each bronchus or bronchiole mingled with the leucocytes of the exudate, but in most instances they are not found in appreciable numbers in the substance of the tissue or in the alveolar contents.

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The lymphatics which run from the pleural network by way of the interlobular septa, bronchial walls, and blood vessel walls to the nodes at the hilum of the lung quickly become a channel for the transport of these bacteria. Great numbers of them are found in these canals and in the sinuses of the lymph nodes at the hilum where they appear to be halted. They cause thrombosis of the lymph channels which become distended to an enormous size and appear to the unaided eye as most conspicuous beaded white strands on the cut surface of the lung extending to connect with the pleural network which may be in places similarly injected and distended with a white infected semipurulent thrombus. These lymphatics are often 2 to 3 mm. in diameter, which is not especially greater than the diameter of the normal channels, but they become conspicuous in a way seldom observed because of their yellowish white contents. Sometimes they might almost be confused with the obstructed bronchi.

It is thought that bacteria extend by growth along these obstructed channels in both directions and thus passing from the lung to the pleura (in a direction opposed to that of the current in unobstructed lymphatics) infect the walls of the pleural cavity and set up the intense inflammation with outpouring of fluid exudate. The pleura itself and all the interlobular septa become edematous and permeated by a serofibrinous exudate with wandering cells.

From the beginning of the infection of the pleura the effusion of fluid exudate becomes a dominant feature of the whole process both in the clinical signs and the anatomical changes. It takes place with extraordinary rapidity and compresses the lung to such a degree as to complete the atelectasis.

When the exudate is present in such large quantities as 2 or more liters the lung becomes a completely airless pasty blue clump of tissue which is usually plastered against the pericardium or back against the side of the vertebral column. The idea that the opening of the chest with the production of pneumothorax could accentuate the collapse of that lung seems rather bizarre, but its ill effects may well come from the influence on the rest of the respiratory tract.

Later the pleural exudate becomes more distinctly purulent, having begun as a thin greenish brown turbid fluid filled with streptococci and disintegrated leucocytes and shreds of fibrin.

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Rapid organization of the inflammatory exudate is everywhere characteristic. This affects the alveoar and bronchial contents and they are replaced in part by connective tissue. It results particularly in interstitial new growth of connective tissue which thickens the alveolar walls, the bronchial walls, the adventitia of blood vessels, and the interlobular septa. The thrombosed lymphatics become organized and occluded permanently by fibrous tissue so that new ones must eventually be formed, and absorption in the meanwhile is greatly hampered.

Most striking of all is the rapid organization of the thick layer of fibrin which generally covers the pleura. This results in the formation of thick red vascular granulation tissue on the pleural surface. Adhesions between contiguous surfaces are quickly rendered permanent and in the later stages encapsulated pockets of intrapleural origin filled with pus are not infrequently formed and offer difficulties to the surgeon.

Occasionally large portions of the inflamed lung become necrotic. Such necrotic material is loaded with streptococci and is often discharged through the bronchus, leaving a cavity. When this cavity communicates with the pleura too, pneumothorax may result, or if the chest is already open it appears as a bronchopleural fistula.

Such a disease of the lung betrays at every point its tendency to heal. Everything described above, except perhaps the bronchial exudate, the pleural exudate, and the intrapulmonary necroses or abscesses, partakes of the nature of a barricading process. All the changes tend to limit the advance of the streptococci and indurate the tissue everywhere to this end. The alveolar exudate with its dense fibrin later replaced by connective tissue, the thrombosis of the lymphatics, the thickening and granulation tissue formation in the bronchial walls, interlobular septa, and pleura, and the widespread hyperplasia of lymphoid tissue throughout the lung are all evidences of a considerable power of resistance which allows the body time for defence. The infection is fairly well localized in the respiratory tract and there is no septicemia until perhaps the last few hours of life. Other organs therefore suffer little. The upper respiratory tract is all infected, and ulcerative changes have been described.

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The second type, designated arbitrarily lobular pneumonia, is composed of cases in which the streptococci invade in the same way. One does not know how to distinguish the symptoms and yet at autopsy although sometimes even the lungs may look much the same at a casual glance they are really different. There are no firm peribronchial nodules. Instead there are patches of consolidation in which the alveoli are filled with blood and leucocytes and enormous quantities of streptococci. No interstitial changes are there and no signs of resistance; widespread necrosis occurs with final destruction of areas of lung substance. Hemorrhage about these areas is usual and there is often pleural effusion but without any organization of the exudate. There are many cases in which this lobular pneumonia occurs in the pure form, but there are many others in which it is found side by side with the interstitial bronchopneumonia. They are different expressions of reaction to the same infection, but in these the reaction is very feeble. There is nothing new in the forms of pneumonia in this epidemic. They have evidently existed always and with a fair degree of probability one may trace them back to the 16th century. More recognizable descriptions date from 1812, and perfectly clear ones from Delafield in 1884.

Addendum.

Significance of the Presence of Influenza Bacilli.

Since this paper was sent to press another and much greater epidemic has occurred with appalling mortality from pneumonia. The original disease in this epidemic has been spoken of as influenza, and measles has played no part. Attention has been concentrated upon the influenza bacillus of Pfeiffer since it is commonly regarded as the cause of influenza, and much new information has already been published as to the biology of that organism.

Whatever its true status in connection with the epidemic disease, influenza, we have at least learned from numerous autopsies that it must be regarded as a serious pathogenic agent in the production of pneumonia and that it may be found in pure culture associated with a form of pneumonia which is practically identical with the inter-

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stitial bronchopneumonia described above, except in the absence of empyema. It is, however, often found with pneumococci and streptococci in other types of pneumonia.

The invention of a new stain for Gram-negative bacteria by Dr. Goodpasture and its successful combination with Weigert's stain for Gram-positive organisms have made it possible to restudy the tissues from the epidemic described above with the assurance of being able to demonstrate influenza bacilli in the tissues whenever they were present and to distinguish them easily from streptococci, pneumococci, and other Gram-positive bacteria. This rests, of course, entirely upon the basis of their morphology, but in many cases it is supported by the results of cultures from sputum or even from the lungs.

I have, therefore, taken the opportunity afforded in the correction of the proof to introduce notes on the presence of these organisms, although the general discussion is left unchanged.

It is evident that owing to unsatisfactory culture methods influenza bacilli were missed in many cases, and it is now proved that the bacilli can be demonstrated in the bronchioles and occasionally in the alveoli of the lungs in 16 of 48 acute cases, while in at least 6 other cases they were present in the sputum. Their distribution among the groups of cases is interesting.

Type of pneumonia.	Total No. of cases.	Influenza bacilli present in.	Case Nos.
Interstitial bronchopneumonia	16	5	15, 32, 37, 49, 191
" and lobular pneumonia	9	4	29, 35, 181, 205
Lobular pneumonia	7	0	
Lobar "	11	5	33, 45, 51, 186, 188
Interstitial bronchopneumonia and lobar pneumonia	5	2	23, 180

It may be said that they tend to be associated with the interstitial and organizing processes, since even some of the cases of lobar pneumonia (Nos. 45, 186, and 188) show a tendency to organization of the exudate and thickening of the interstitial tissue. One might leap to the conclusion that they are responsible for this process or even that they are the forerunners of the streptococcus and pneumococcus in-

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fections. It is even suggested in the face of the obvious influence of the epidemic of measles that during the whole period of the winter epidemic there may have been influenza which predisposed to secondary streptococcus infections. But there remain the facts that most of the cases show no influenza bacilli and that in those which are most typical of the form of interstitial bronchopneumonia (Nos. 34, 41, 184, etc.) the most painstaking search through many sections has failed to reveal any of these organisms. It is true that Case 37 shows relatively few streptococci and great numbers of influenza bacilli and is probably to be regarded as essentially produced by the influenza bacillus. But in all the others the streptococcus is the predominant organism, if we except Case 196 in which there were no influenza bacilli and in which the lesion seems to have been caused by pneumococci.

I think it must be recognized that the interstitial forms of bronchopneumonia can be produced by various organisms, including pneumococci, streptococci, and the influenza bacillus. Where there is a mixed infection it is difficult to assign to each its exact part in the process, but it appears that in spite of the frequent presence of the influenza bacillus this was essentially an epidemic of streptococcal pneumonia.

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EXPLANATION OF PLATES.

PLATE 1.

FIG. 1. Case 14. Interstitial bronchopneumonia. Early bronchial lesion with surrounding hemorrhage.

PLATE 2.

FIG. 2. Case 14. Interstitial bronchopneumonia. Early bronchial lesion. Beginning organization of exudate in bronchial lumen.

PLATE 3.

FIG. 3. Case 15. Interstitial bronchopneumonia. Infiltration of alveolar walls and perivascular tissue.

PLATE 4.

FIG. 4. Case 16. Interstitial bronchopneumonia. Right lung with interlobar empyema pocket.

PLATE 5.

FIG. 5. Case 16. Interstitial bronchopneumonia. Atelectasis with organization of bronchial exudate.

PLATE 6.

FIG. 6. Case 32. Interstitial bronchopneumonia. Early bronchial and peribronchial lesion.

PLATE 7.

FIG. 7. Case 32. Interstitial bronchopneumonia. Bronchial and peribronchial infiltration.

PLATE 8.

FIG. 8. Case 34. Interstitial bronchopneumonia. Portion of left lung showing prominent interlobular septa and peribronchial nodules.

PLATE 9.

FIG. 9. Case 34. Interstitial bronchopneumonia. Portion of left lung showing prominent interlobular septa and many distended lymph channels which appear as white beaded canals.

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PLATE 10.

FIG. 10. Case 34. Interstitial bronchopneumonia. Interlobular septum with great distension of lymph channels by an infected thrombus.

PLATE 11.

FIG. 11. Case 34. Interstitial bronchopneumonia. Thickening and infiltration of the wall of a small bronchus.

PLATE 12.

FIG. 12. Case 34. Interstitial bronchopneumonia, showing dislodgement of the epithelium of the bronchus, the great thickening and infiltration of the wall, and changes in the adjacent alveoli.

PLATE 13.

FIG. 13. Case 37. Interstitial bronchopneumonia. Right lung, showing the nodular character of the peribronchial lesions. The spleen is included.

PLATE 14.

FIG. 14. Case 37. Interstitial bronchopneumonia. Infiltration of bronchial wall which has lost its epithelium. Dense fibrinous plugs in the adjacent alveoli.

PLATE 15.

FIG. 15. Case 39. Interstitial bronchopneumonia. Right lung.

PLATE 16.

FIG. 16. Case 41. Interstitial bronchopneumonia. Left lung.

PLATE 17.

FIG. 17. Case 41. Interstitial bronchopneumonia. Right upper lobe showing large nodules of consolidation about the bronchi.

PLATE 18.

FIG. 18. Case 41. Interstitial bronchopneumonia. Bronchial thickening produced by lymphoid hyperplasia and great infiltration of the wall.

PLATE 19.

FIG. 19. Case 41. Interstitial bronchopneumonia. Infiltration of bronchial wall. Consolidation of adjacent tissue.

PLATE 20.

FIG. 20. Case 41. Interstitial bronchopneumonia. Small bronchus with thickened and hyperemic wall. Surrounding consolidation.

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PLATE 21.

FIG. 21. Case 178. Interstitial bronchopneumonia. Early stage with peribronchial hemorrhages.

PLATE 22.

FIG. 22. Case 178. Interstitial bronchopneumonia following measles. Ulceration of vocal cords.

PLATE 23.

FIG. 23. Case 178. Section passing through pleura and interlobular septum with lymphatic canal, showing valves directed away from the pleura.

PLATE 24.

FIG. 24. Case 178. Interstitial bronchopneumonia. Bronchus with thickened wall, showing masses of streptococci in the purulent contents of the lumen. Infiltration of adjacent alveolar walls.

PLATE 25.

FIG. 25. Case 184. Interstitial bronchopneumonia. Left lung.

PLATE 26.

FIG. 26. Case 184. Interstitial bronchopneumonia following measles. Ulcerative laryngitis. Ulcers of vocal cords and epiglottis.

PLATE 27.

FIG. 27. Case 184. Interstitial bronchopneumonia. Necrosis of mucosa of bronchus. Infiltration and edema of bronchial wall. Infiltration and collapse of adjacent alveoli.

PLATE 28.

FIG. 28. Case 184. Interstitial bronchopneumonia. A mitotic figure is shown in an epithelial cell of the alveolar lining.

FIG. 29. Case 184. Interstitial and lobular pneumonia. Bronchial wall with hyperemia and infiltration and necrosis of the mucosa. Nearby is a patch of lobular pneumonia.

PLATE 29.

FIG. 30. Case 191. Interstitial bronchopneumonia. Left lung.

PLATE 30.

FIG. 31. Case 29. Interstitial bronchopneumonia. Thickening, infiltration, and hyperemia of bronchial wall.

PLATE 31.

FIG. 32. Case 29. Interstitial bronchopneumonia. Infiltration of bronchial wall and adjacent tissue.

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PLATE 32.

FIG. 33. Case 29. Interstitial bronchopneumonia. Induration of interlobular septum and of alveolar walls. Thrombosed lymphatic in the septum.

PLATE 33.

FIG. 34. Case 29. Interstitial bronchopneumonia. Infiltration of bronchial wall. Consolidation of adjacent tissue.

PLATE 34.

FIG. 35. Case 181. Interstitial bronchopneumonia. Right lung with cavity in the upper lobe and bronchiectases in the lower.

PLATE 35.

FIG. 36. Case 194. Interstitial bronchopneumonia, combined with lobular pneumonia. Hemorrhagic lobular area in lower lobe.

PLATE 36.

FIG. 37. Case 205. Bilateral hyaline degeneration of rectus abdominis muscle with rupture and hemorrhage.

PLATE 37.

FIG. 38. Case 205. Interstitial bronchopneumonia. Left lower lobe with projecting peribronchial nodules.

PLATE 38.

FIG. 39. Case 205. Combined interstitial bronchopneumonia and lobular pneumonia.

PLATE 39.

FIG. 40. Case 20. Lobular pneumonia with large area of necrosis and hemorrhage. Distended lymphatics run to the pleural surface.

PLATE 40.

FIG. 41. Case 26. Lobular pneumonia with empyema. Distended lymphatics run to the pleural surface. Left lung.

PLATE 41.

FIG. 42. Case 55. Lobular streptococcal pneumonia with extensive necroses and empyema. Left lung.

PLATE 42.

FIG. 43. Case 55. Lobular streptococcal pneumonia with abscesses. Right lung.

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PLATE 43.

FIG. 44. Case 187. Lobular streptococcal pneumonia. The consolidation is confluent in the upper lobe but focal in the lower part of the lung. Left lung.

PLATE 44.

FIG. 45. Case 187. Confluent lobular streptococcal pneumonia. Hyaline thrombi in alveolar capillaries.

FIG. 46. Case 187. Lobular streptococcal pneumonia. One alveolus from the preparation shown in Fig. 45. The hyaline fibrinous thrombi in the capillaries stain deeply and streptococci are seen with leucocytes in the alveolus.

PLATE 45.

FIG. 47. Case 192. Hemorrhagic lobular pneumonia. Left lung.

PLATE 46.

FIG. 48. Case 192. Hemorrhagic lobular pneumonia. Right lung.

PLATE 47.

FIG. 49. Case 192. Hyaline degeneration in the rectus abdominis muscle.

PLATE 48.

FIG. 50. Case 25. Lobar pneumonia. Pneumococcus infection. Infiltration of alveolar walls with leucocytes.

PLATE 49.

FIG. 51. Case 188. Lobar pneumonia. Pneumococcus Type II and *B. influenzæ*. Right lung.

PLATE 50.

FIG. 52. Case 21. Combination of lobar pneumonia (pneumococcus infection) with interstitial bronchopneumonia (streptococcus infection). Left lung.

PLATE 51.

FIG. 53. Case 31. Typical lobar pneumonia. Pneumococcus Type IV. Left lung. The other lung showed interstitial bronchopneumonia with streptococcus infection.

PLATE 52.

FIG. 54. Case 180. Combined lobar pneumonia and interstitial bronchopneumonia in the same lung. Pneumococcus Type II and streptococcus. Right lung.

PLATE 53.

FIG. 55. Case 196. Interstitial bronchopneumonia. Lobar pneumonia in the opposite lung. Pneumococcus Type II.

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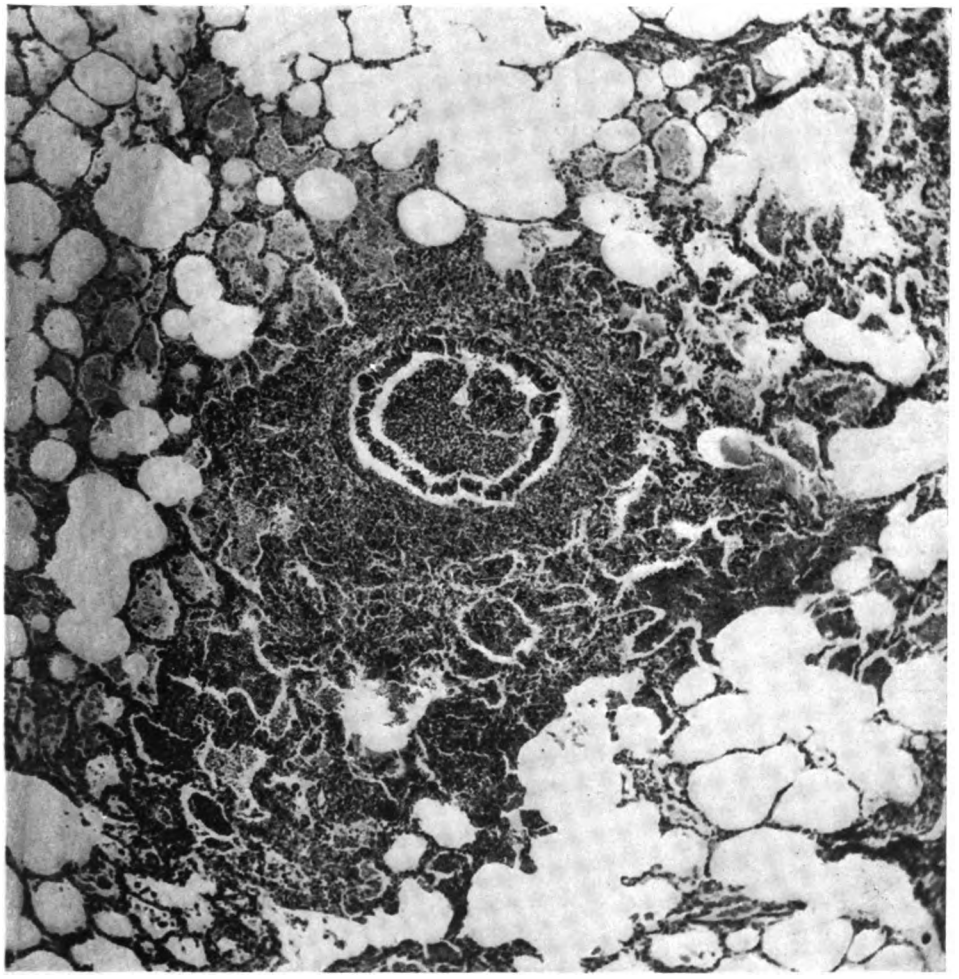

FIG. 1.

(MacCallum: Pneumonia in army camps.)

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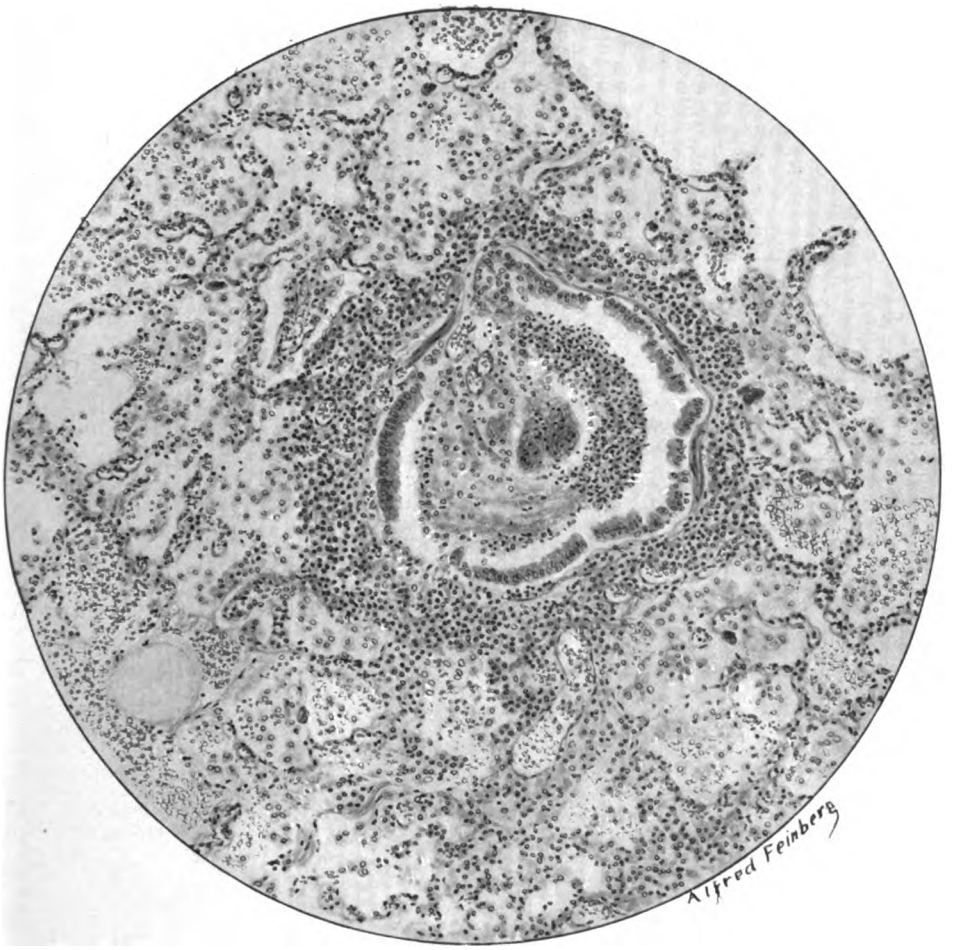

FIG. 2.

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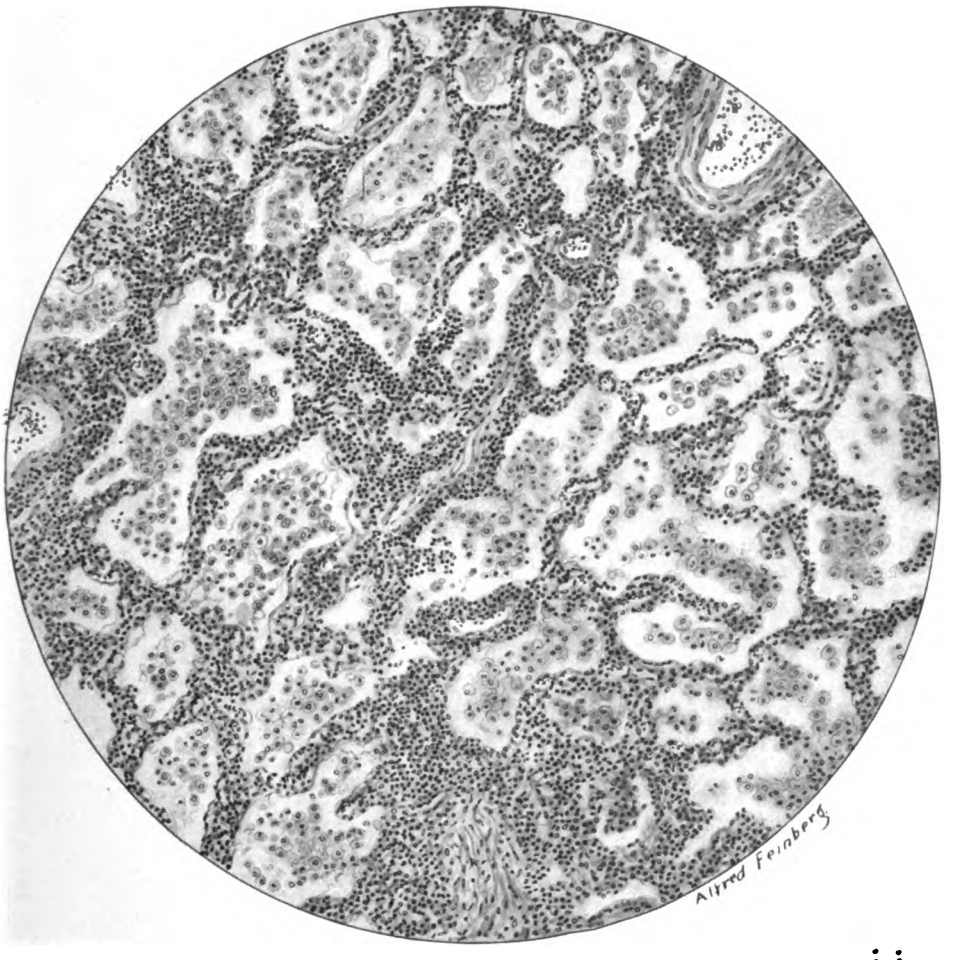

FIG. 3.

(MacCallum: Pneumonia in army camps.)

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FIG. 4.

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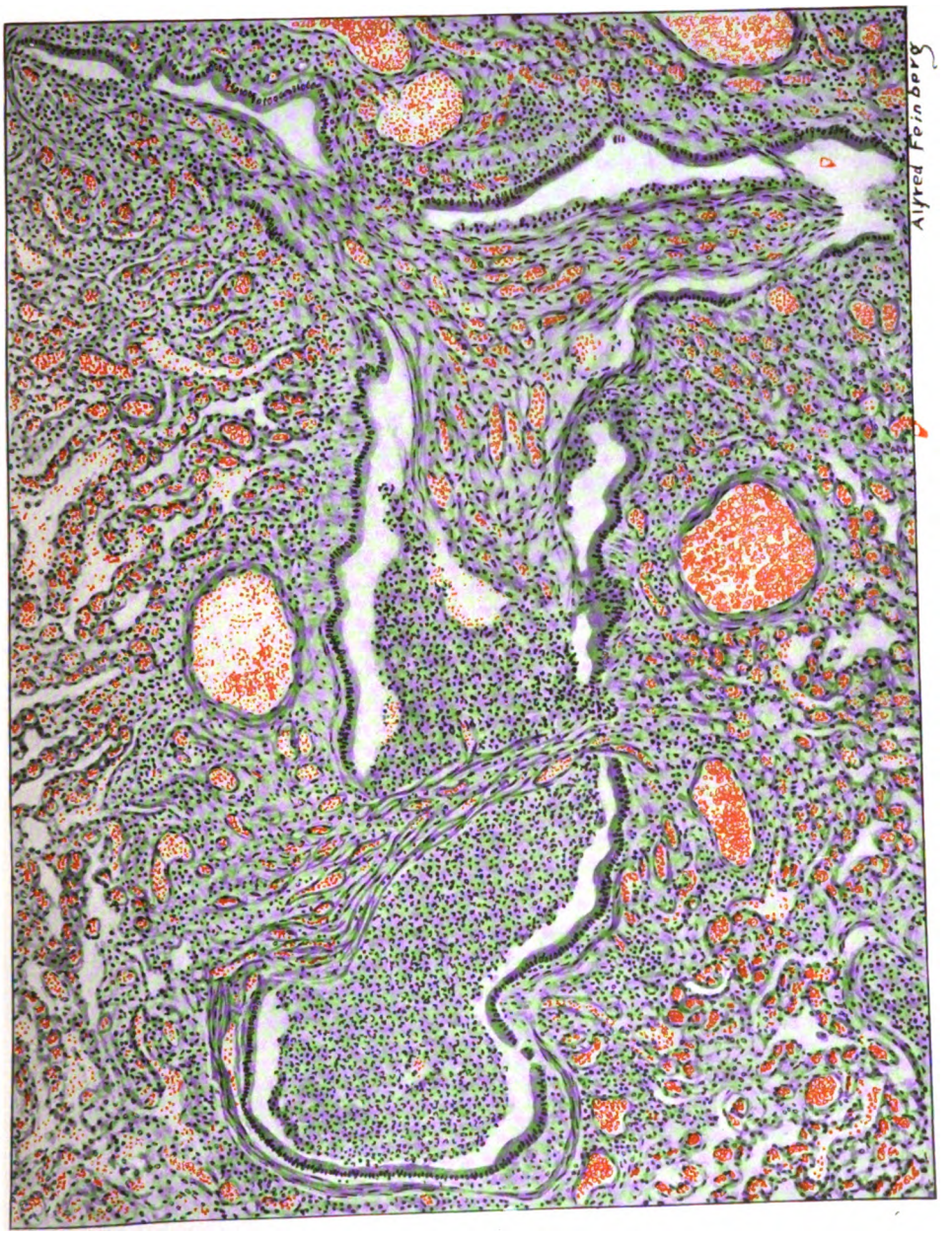

FIG. 5.

(MacCallum: Pneumonia in army camps.)

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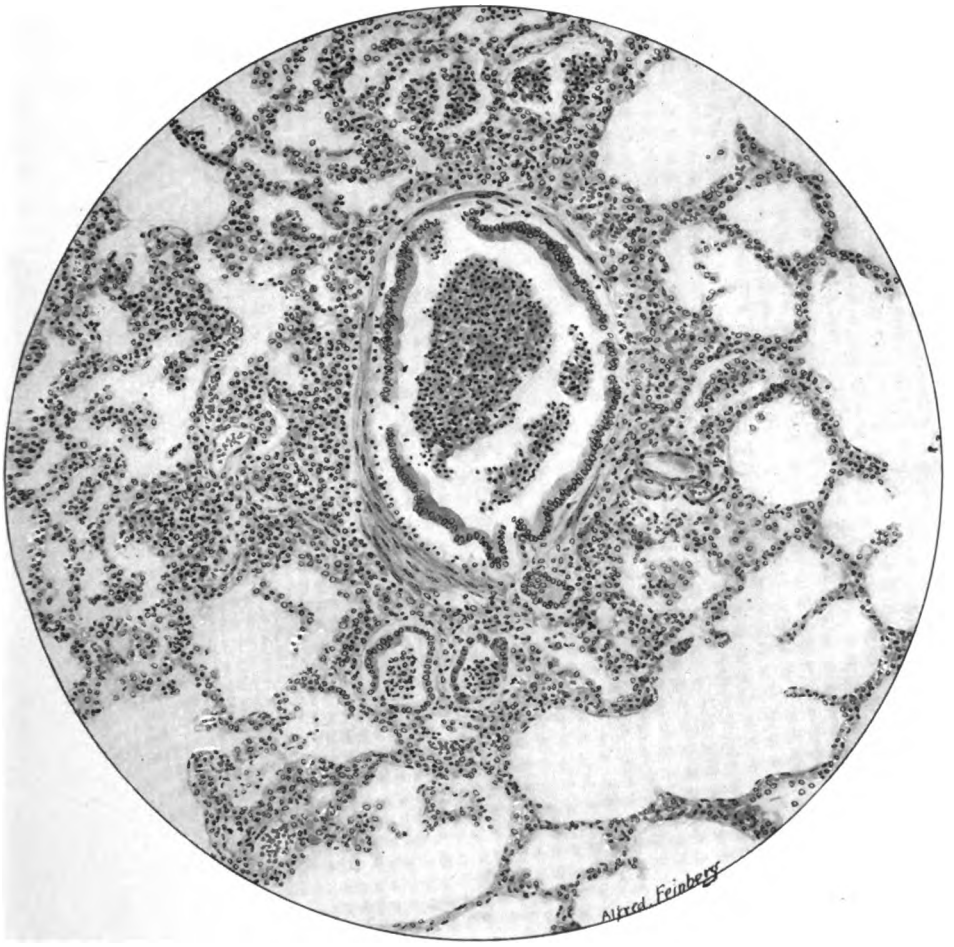

FIG. 6.

(MacCallum: Pneumonia in army camps.)

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FIG. 7.

(MacCallum: Pneumonia in army camps.)

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FIG. 8.

(MacCallum: Pneumonia in army camps.)

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FIG. 9.

(MacCallum: Pneumonia in army camps.)

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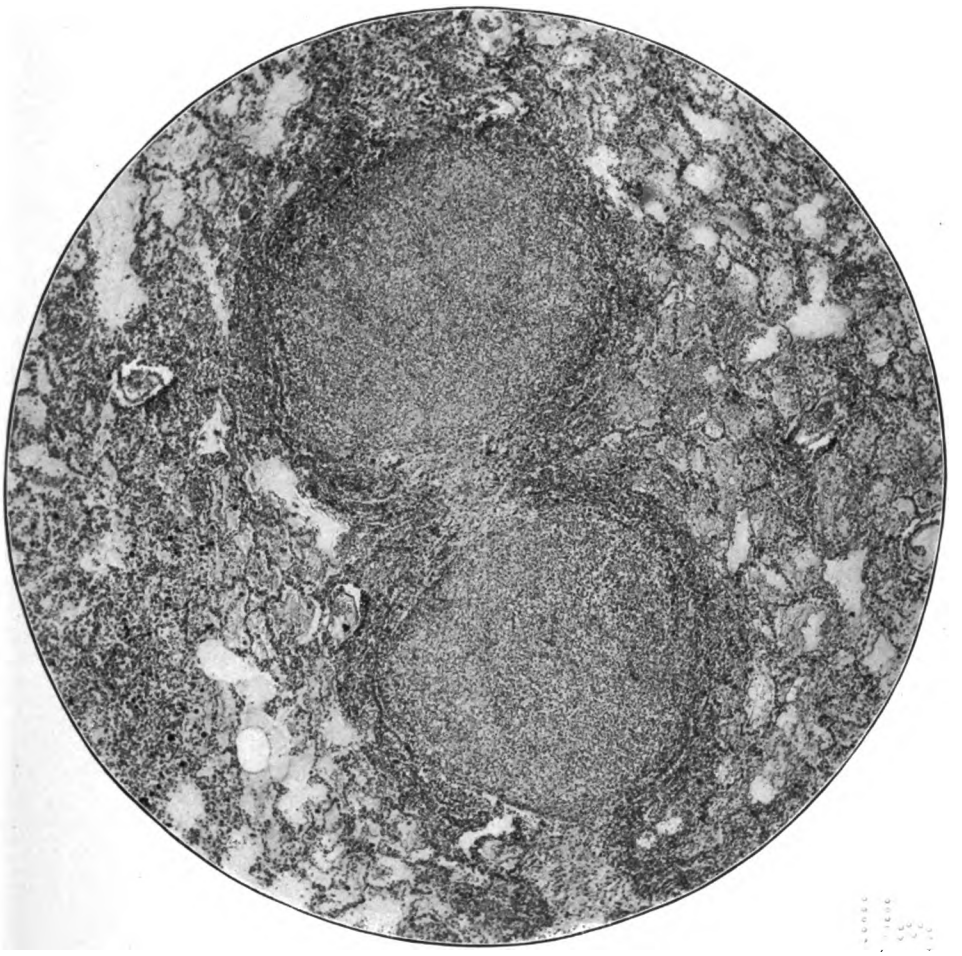

FIG. 10.

(MacCallum: Pneumonia in army camps.)

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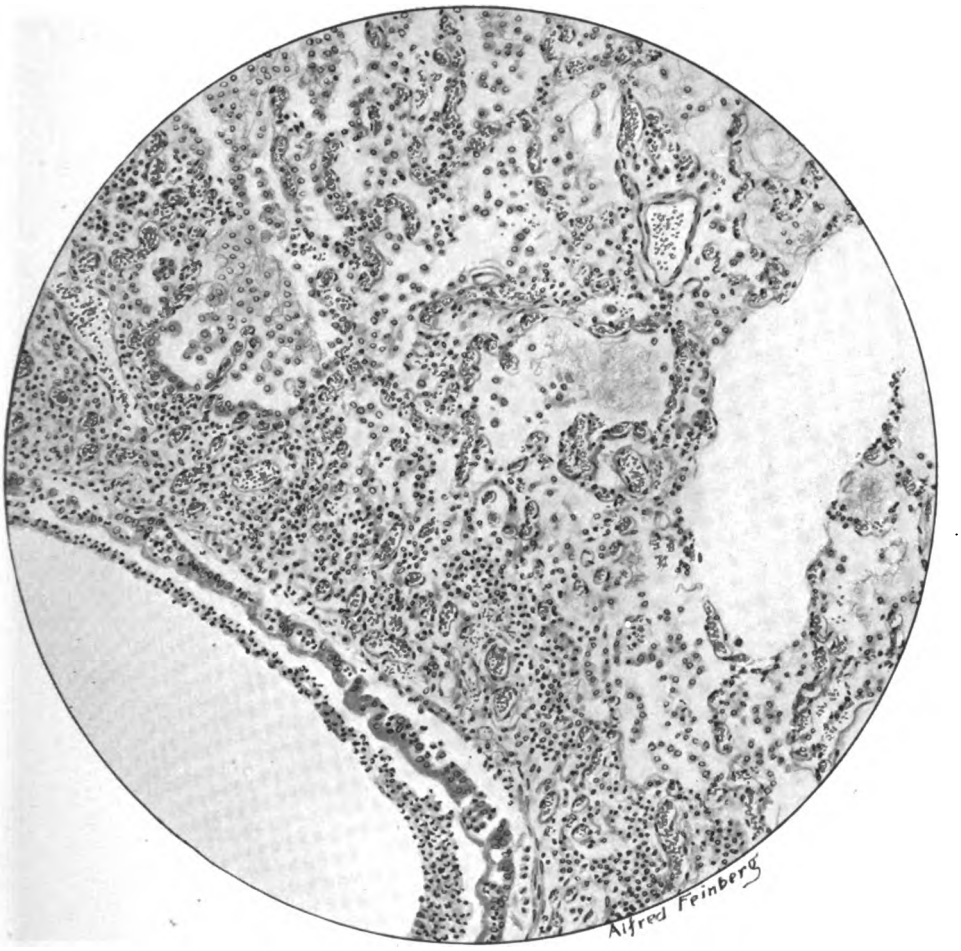

FIG. 11.

(MacCallum: Pneumonia in army camps.)

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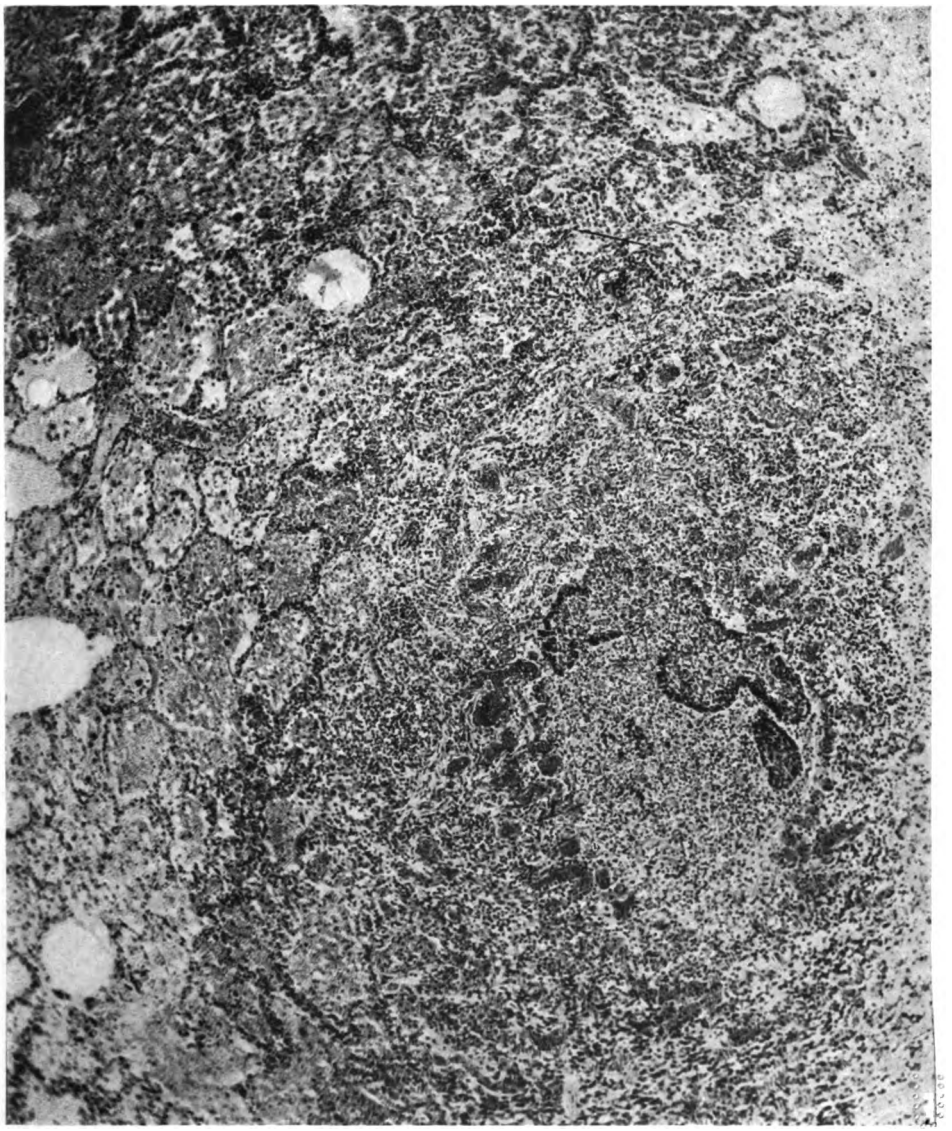

FIG. 12.

(MacCallum: Pneumonia in army camps.)

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FIG. 13.

(MacCallum: Pneumonia in army camps)

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FIG. 14.

(MacCallum: Pneumonia in army camps.)

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FIG. 15.

(MacCallum: Pneumonia in army camps.)

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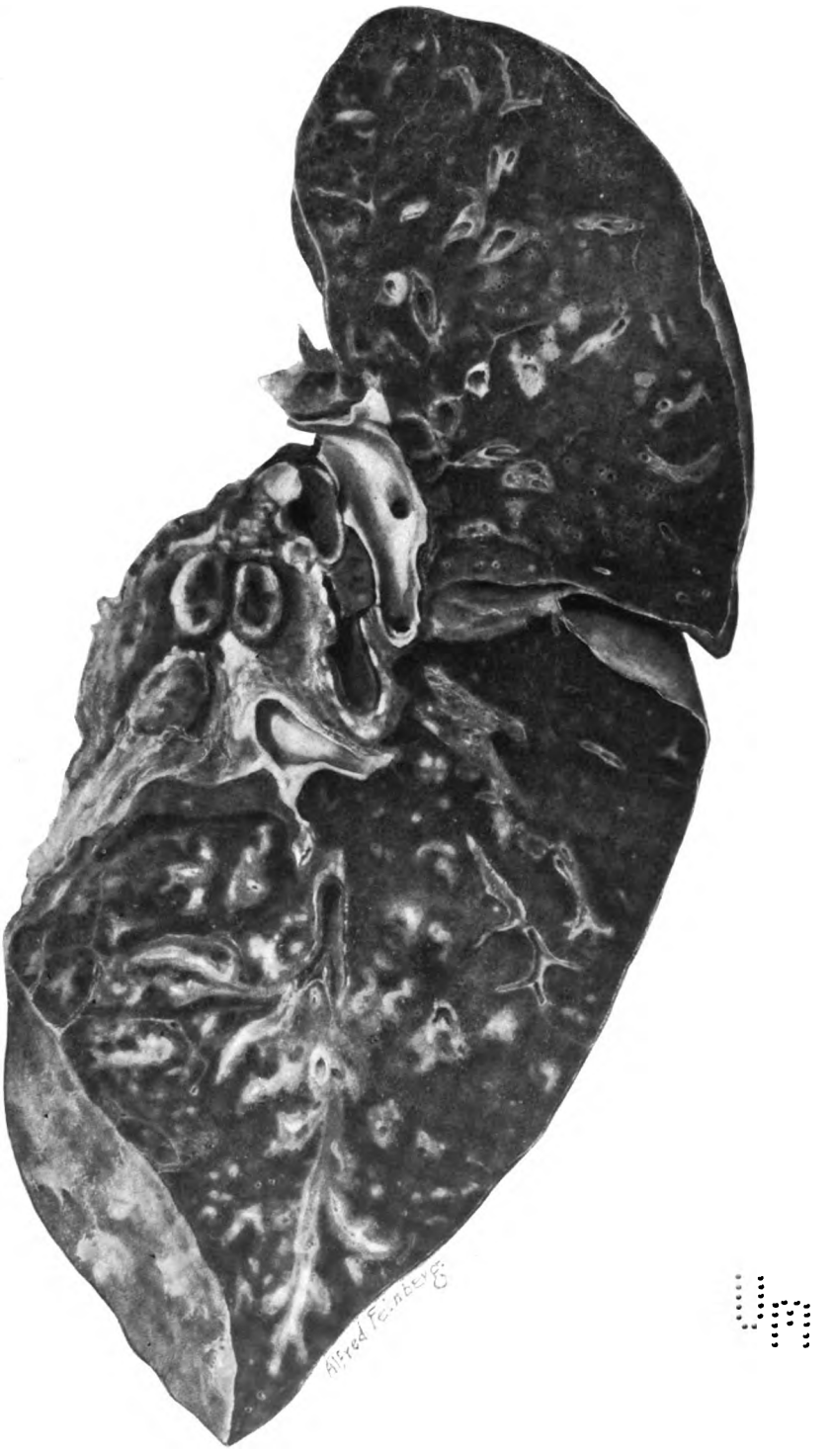

FIG. 16.

(MacCallum: Pneumonia in army camps.)

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FIG. 17.

(MacCallum: Pneumonia in army camps.)

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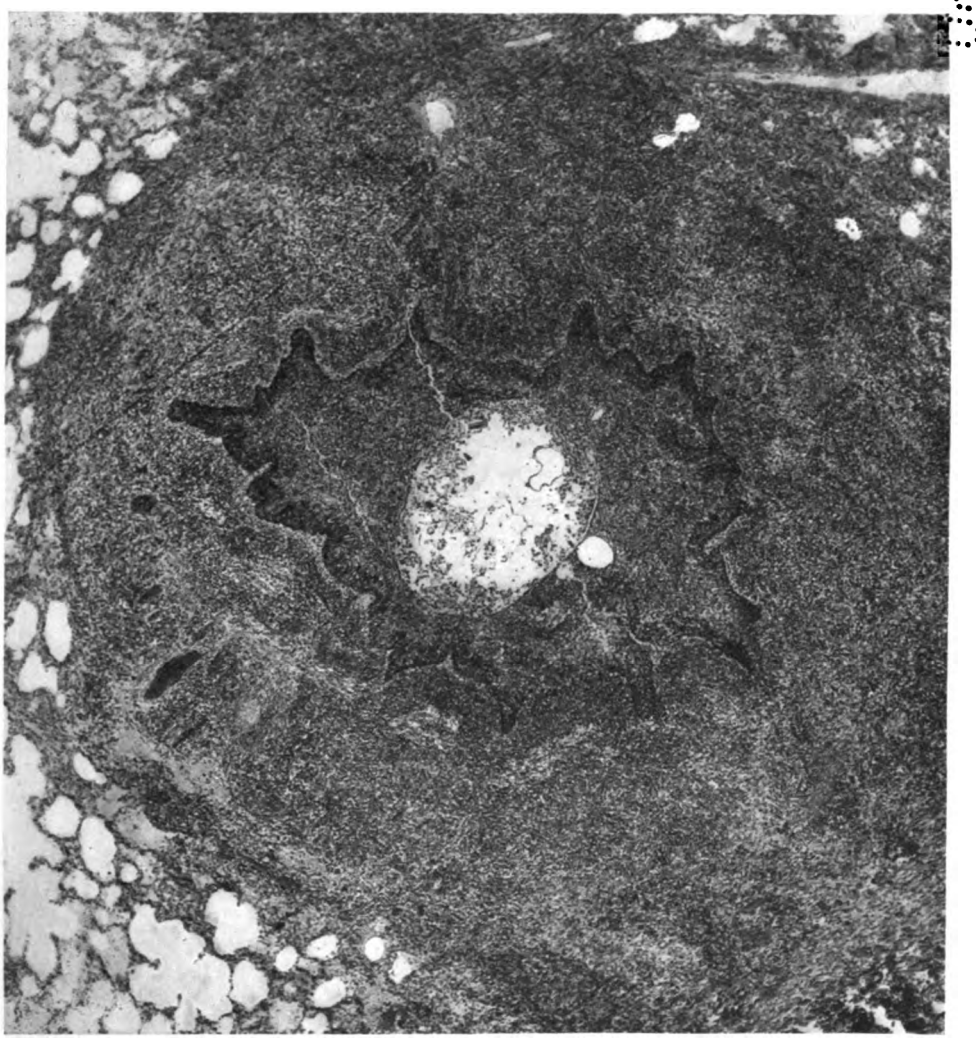

FIG. 18.

(MacCallum: Pneumonia in army camps.)

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FIG. 19.

(MacCallum: Pneumonia in army camps.)

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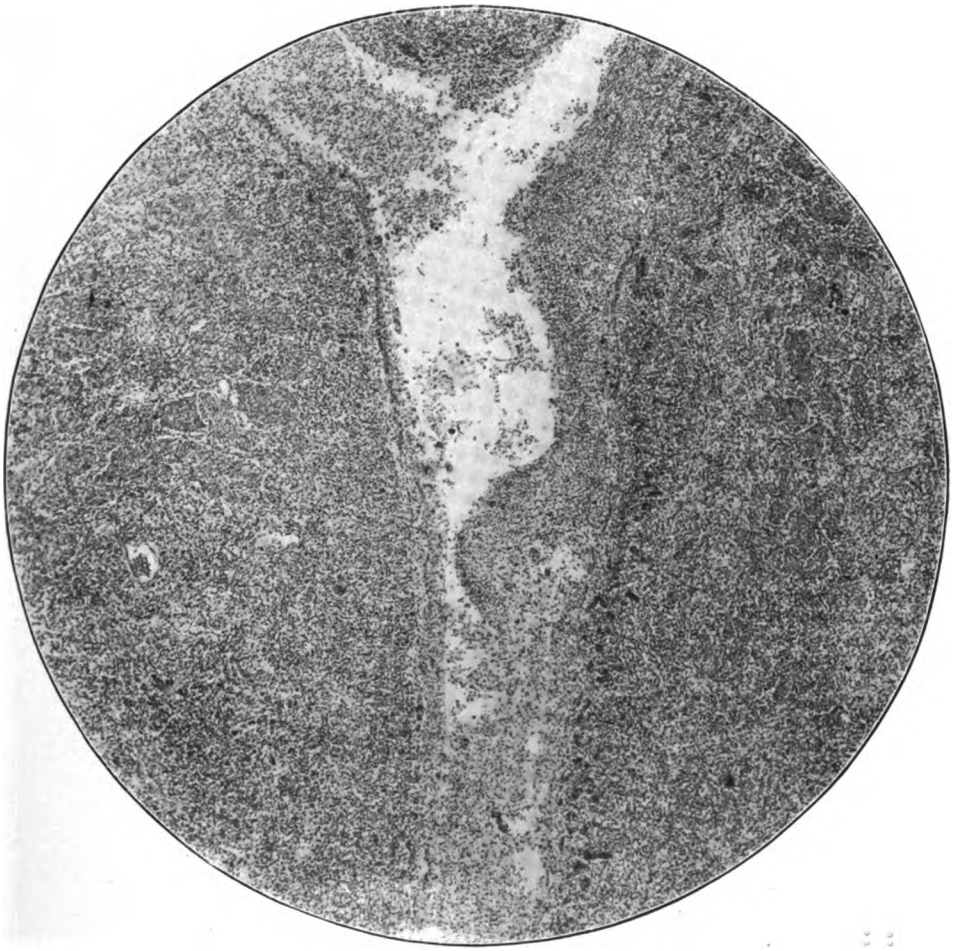

FIG. 20.

(MacCallum: Pneumonia in army camps.)

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FIG. 21.

(MacCallum: Pneumonia in army camps.)

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FIG. 22.

(MacCallum: Pneumonia in army camps.)

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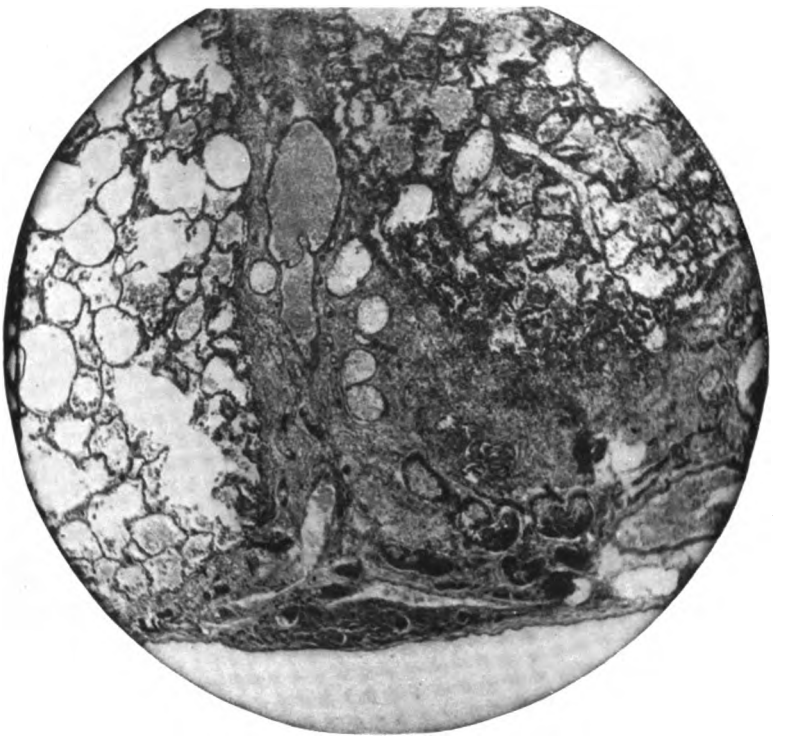

FIG. 23.

(MacCallum: Pneumonia in army camps.)

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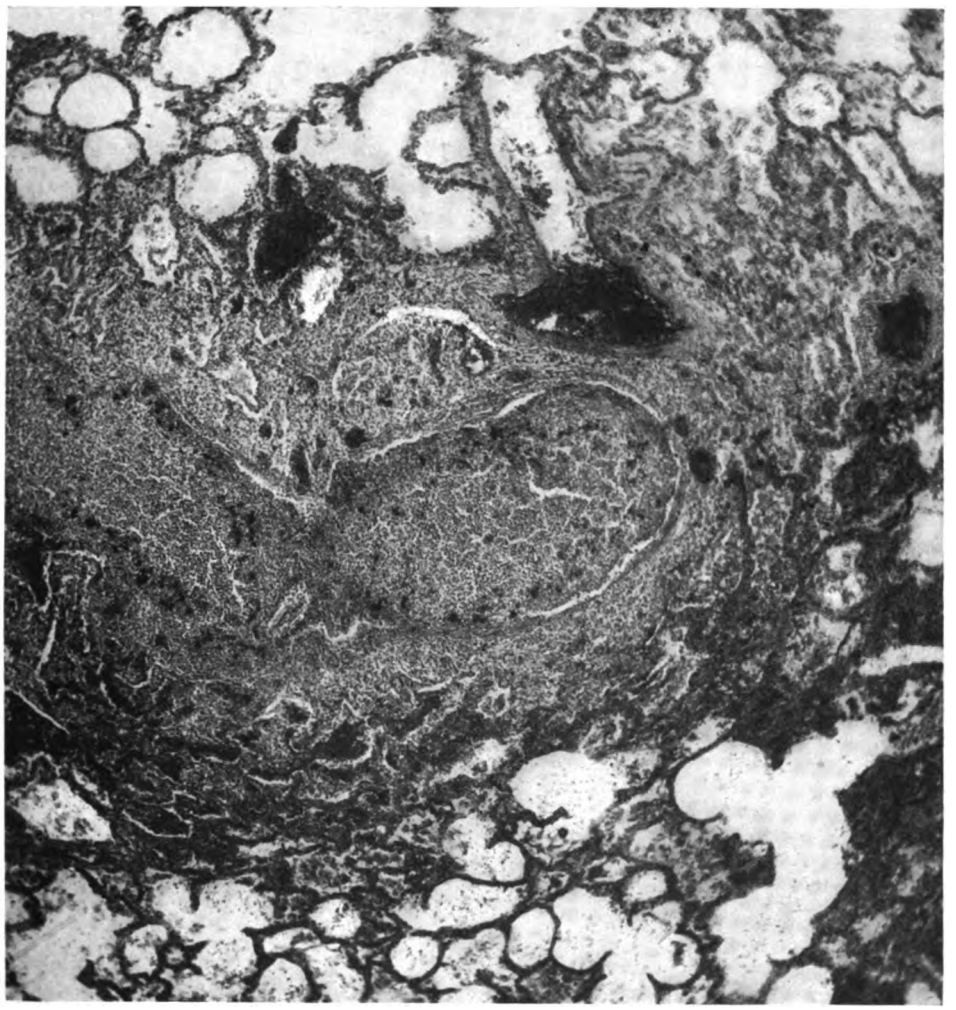

FIG 24.

(MacCallum: Pneumonia in army camps.)

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FIG. 25.

(MacCallum: Pneumonia in army camps)

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FIG. 26.

(MacCallum: Pneumonia in army camps.)

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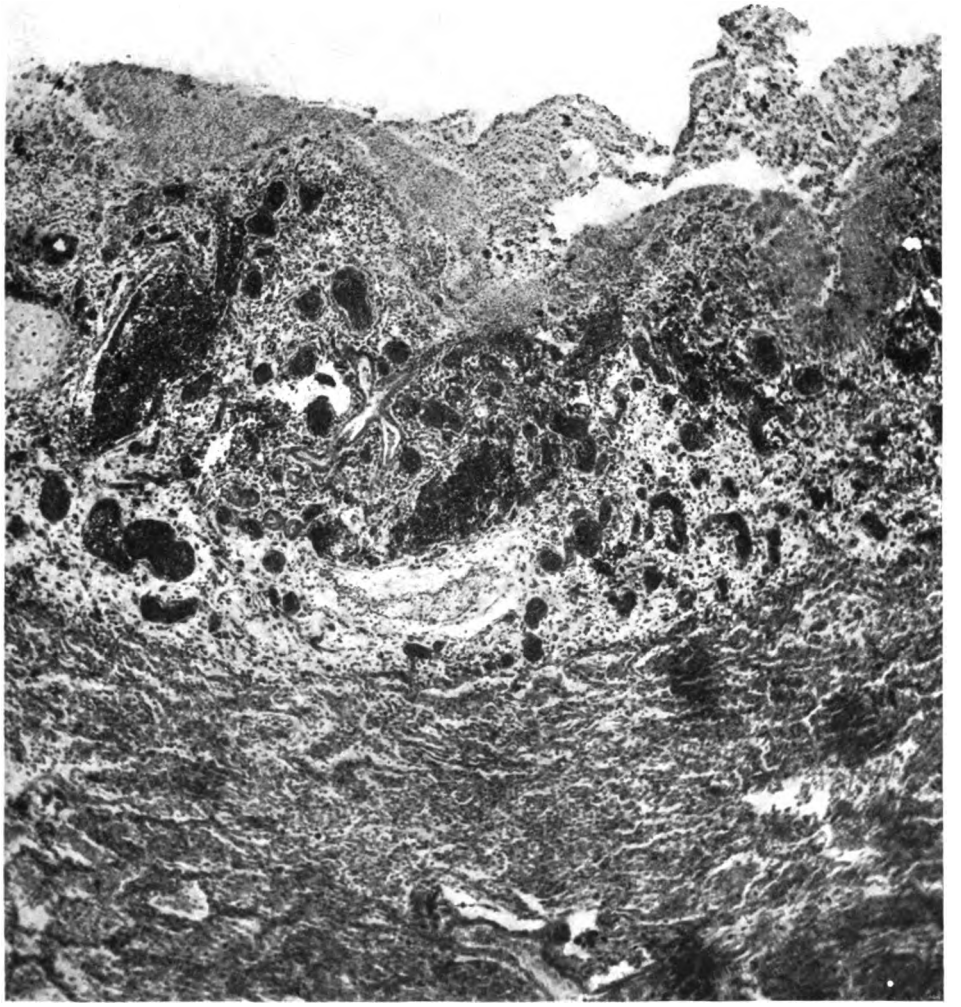

FIG. 27.

(MacCallum: Pneumonia in army camps.)

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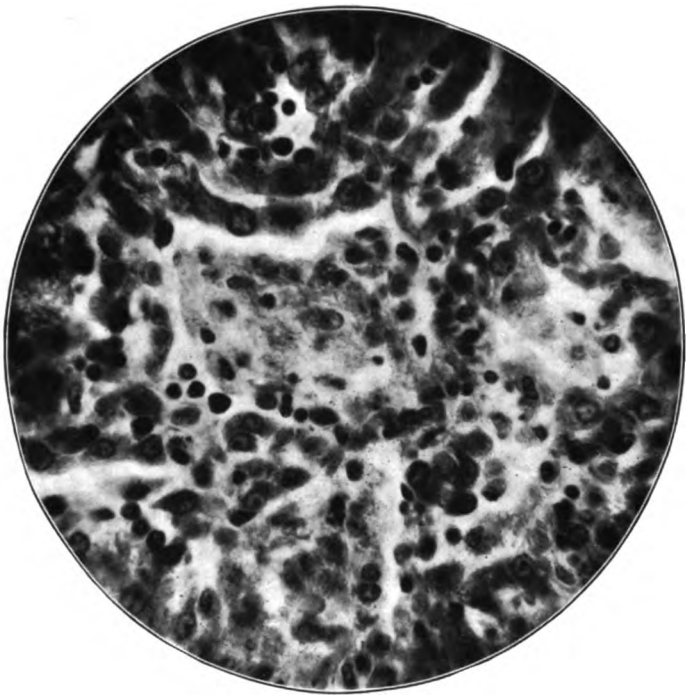

FIG. 28.

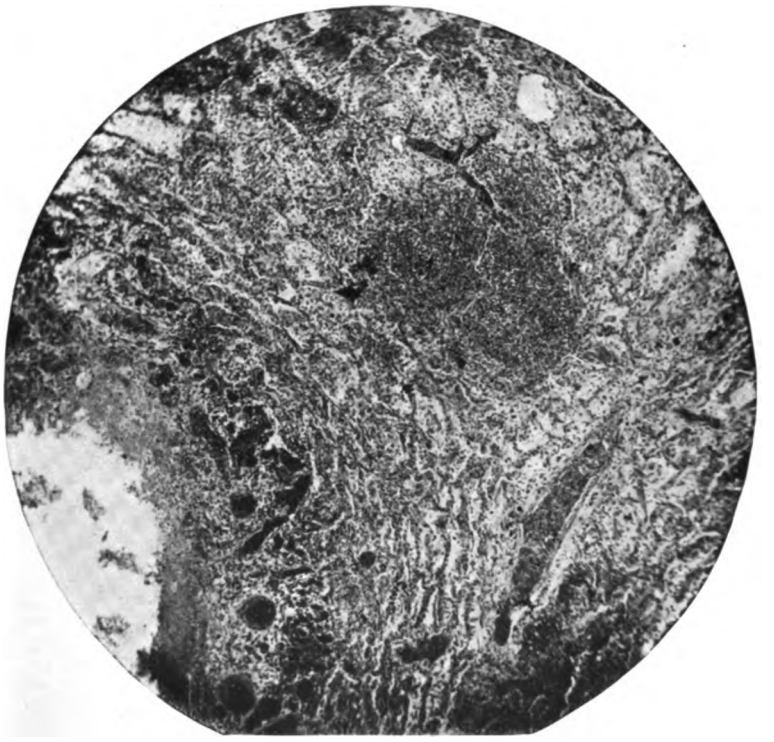

FIG. 29.

(MacCallum: Pneumonia in army camps.)

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FIG. 30.

(MacCallum: Pneumonia in army camps.)

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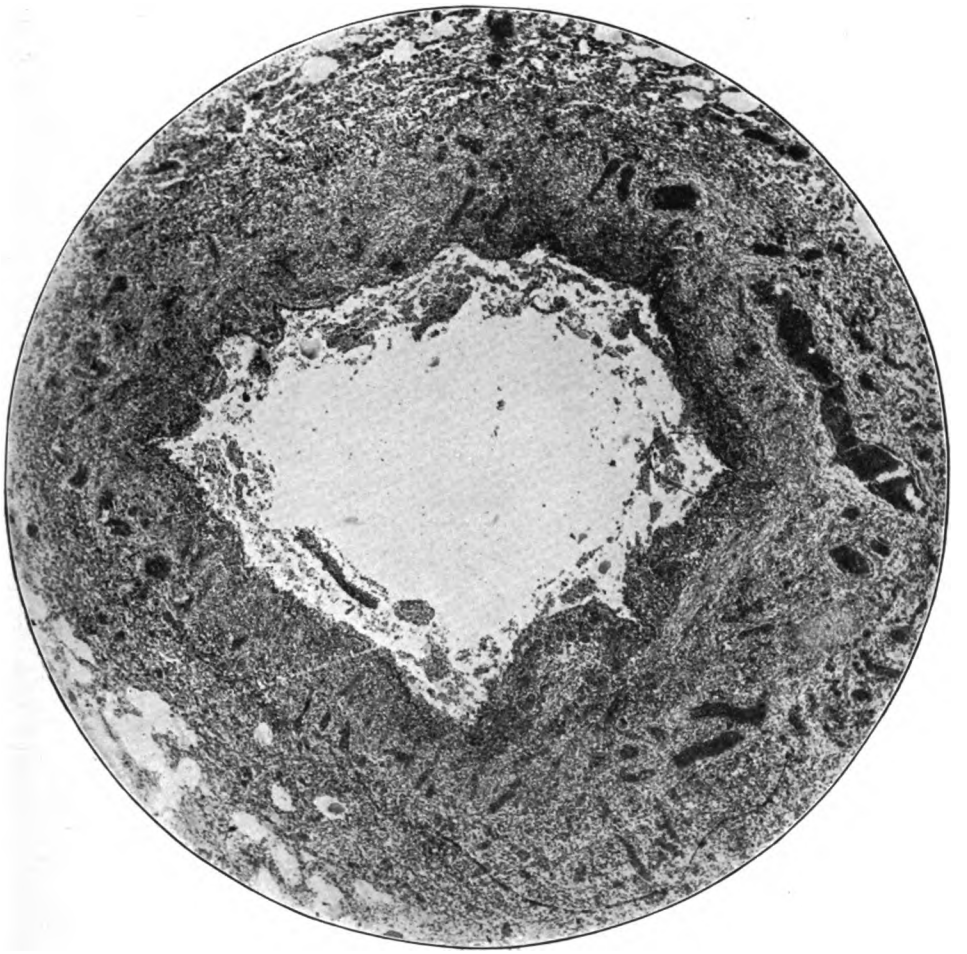

FIG. 31.

(MacCallum: Pneumonia in army camps.)

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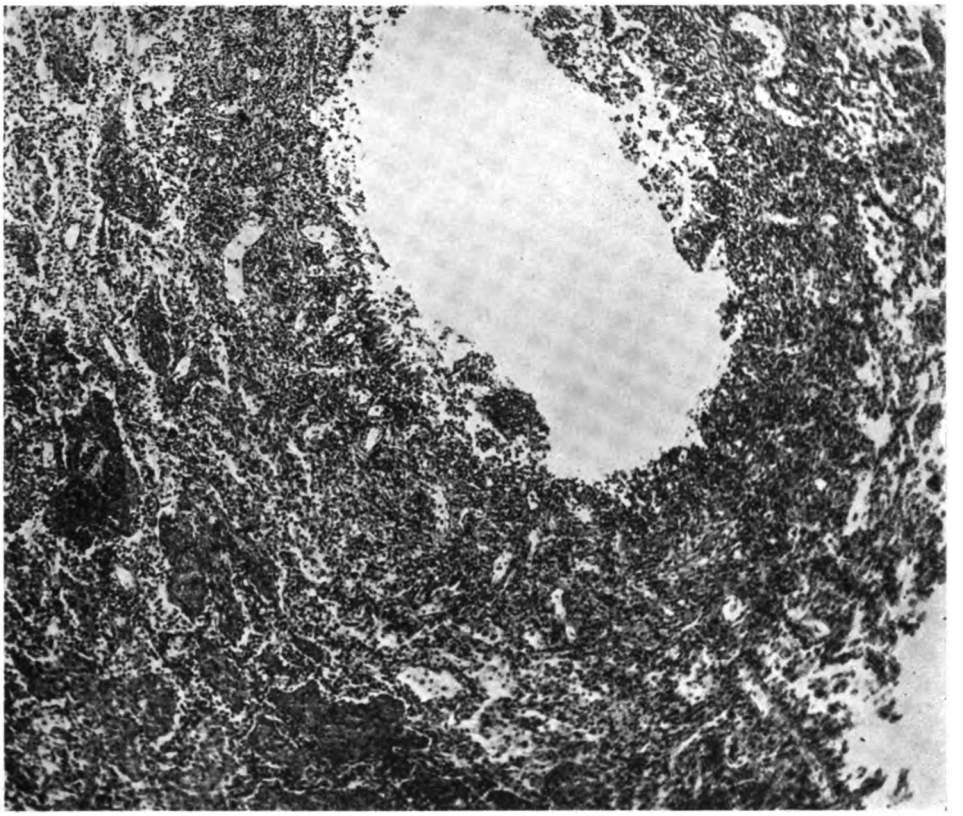

FIG. 32.

(MacCallum: Pneumonia in army camps.)

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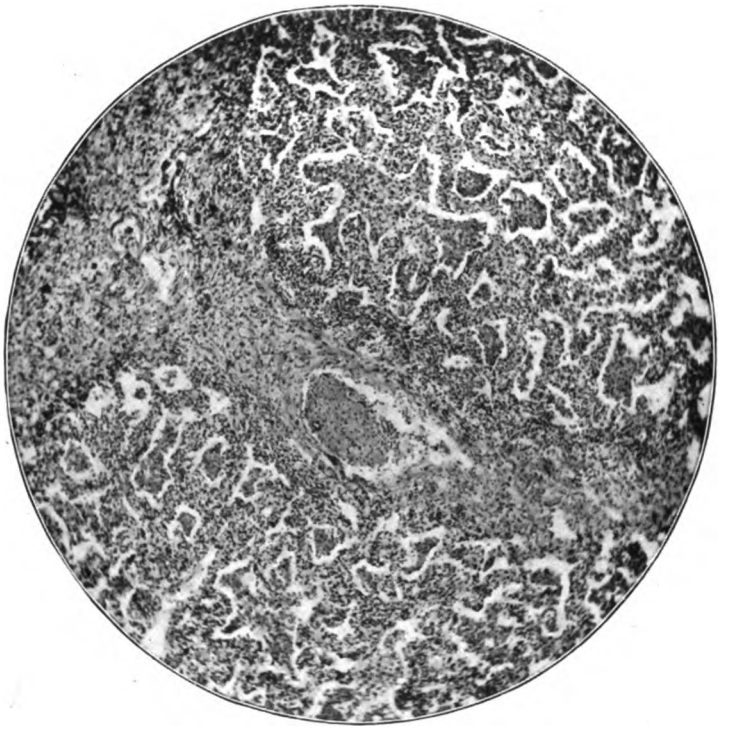

FIG. 33.

(MacCallum: Pneumonia in army camps.)

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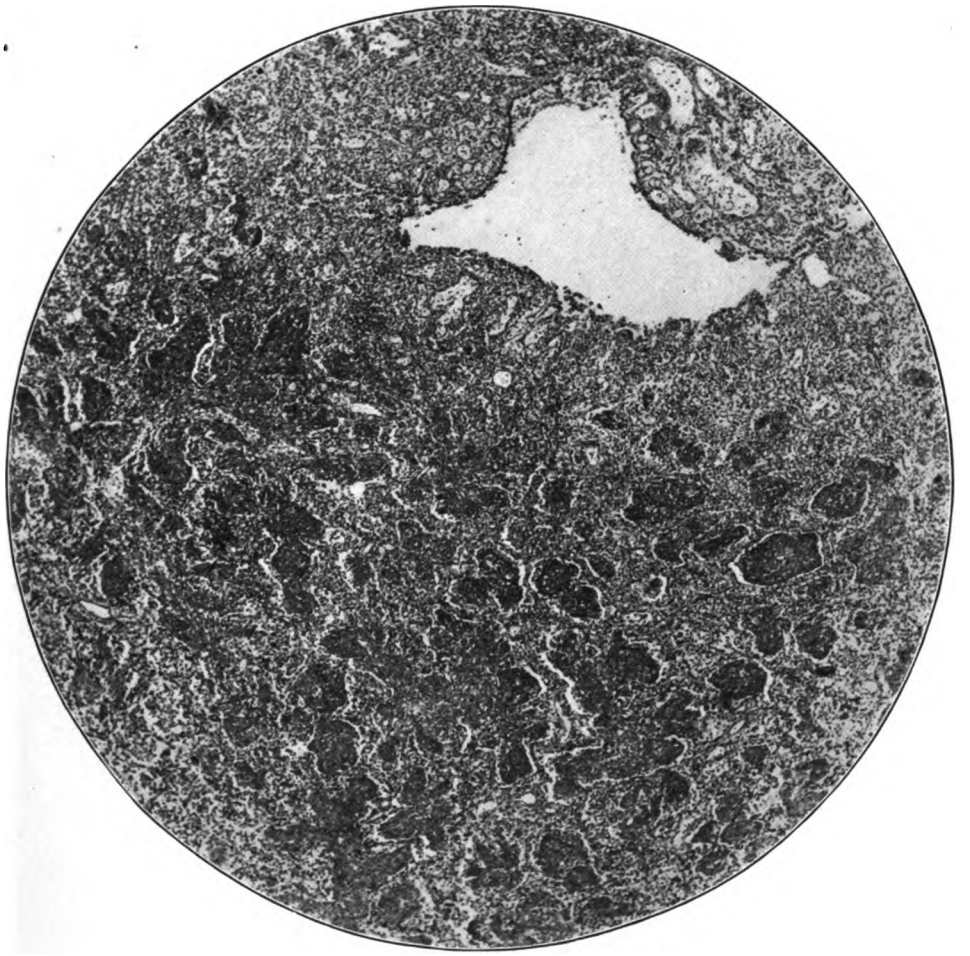

FIG. 34.

(MacCallum: Pneumonia in army camps.)

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FIG. 35.

(MacCallum: Pneumonia in army camps.)

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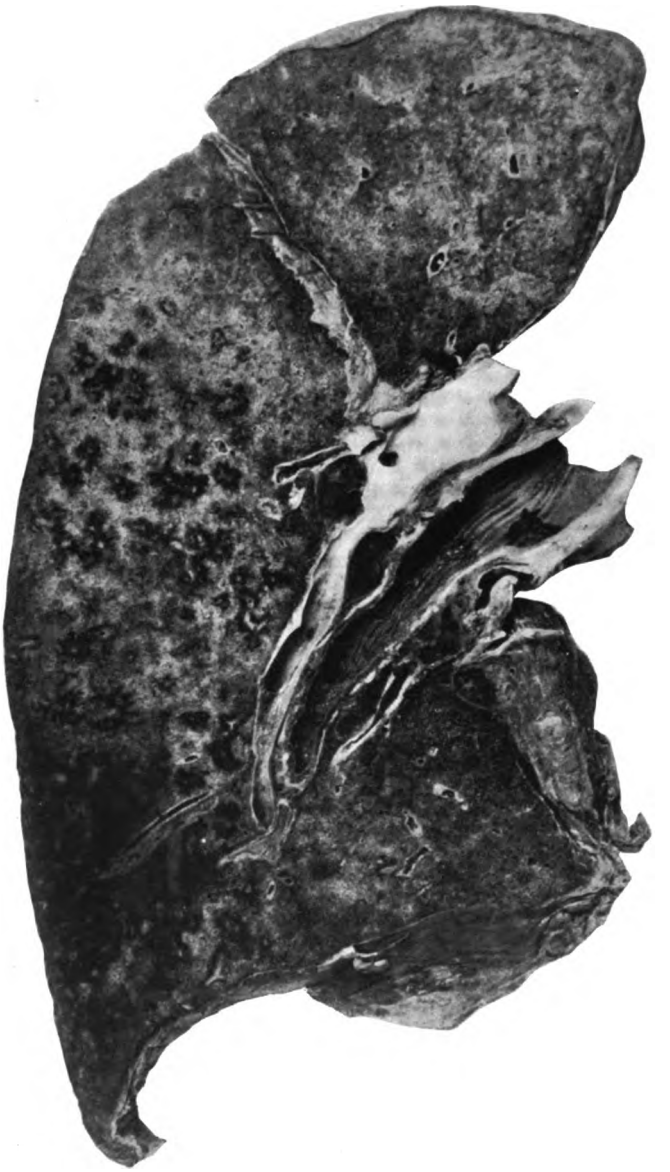

FIG. 36.

(MacCallum: Pneumonia in army camps.)

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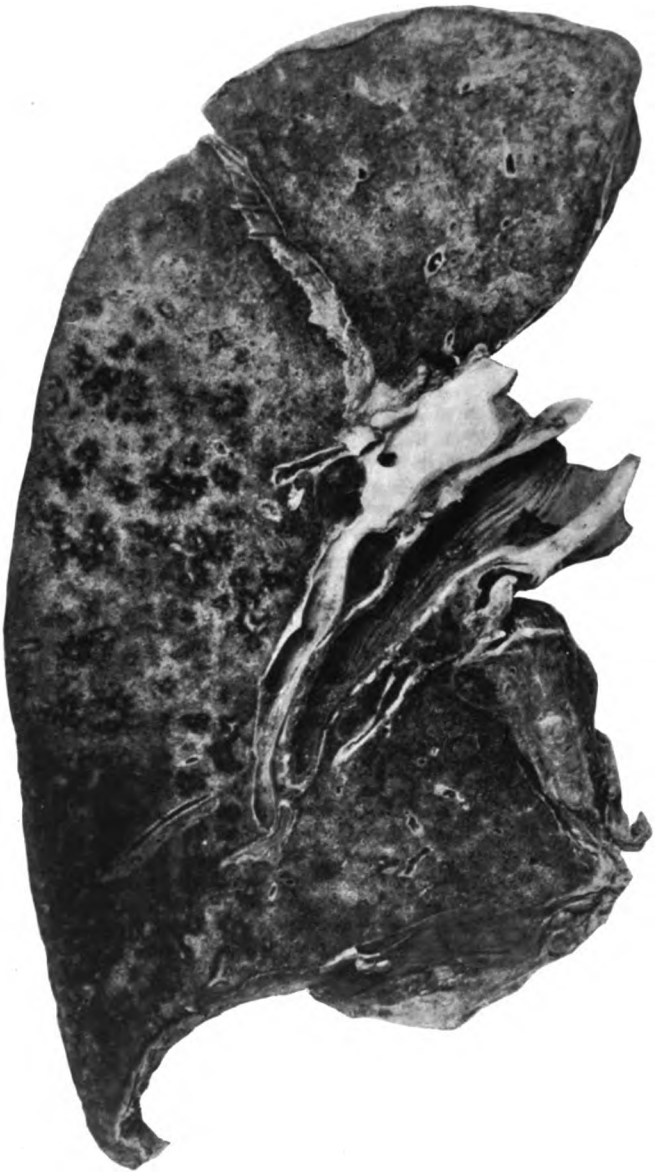

FIG. 36.

(MacCallum: Pneumonia in army camps.)

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FIG. 37.

(MacCallum: Pneumonia in army camps.)

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FIG. 38.

(MacCallum: Pneumonia in army camps.)

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FIG. 39.

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FIG. 40.

(MacCallum: Pneumonia in army camps.)

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FIG. 41.

(MacCallum: Pneumonia in army camps.)

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FIG. 42.

(MacCallum: Pneumonia in army camps.)

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FIG. 43.

(MacCallum: Pneumonia in army camps.)

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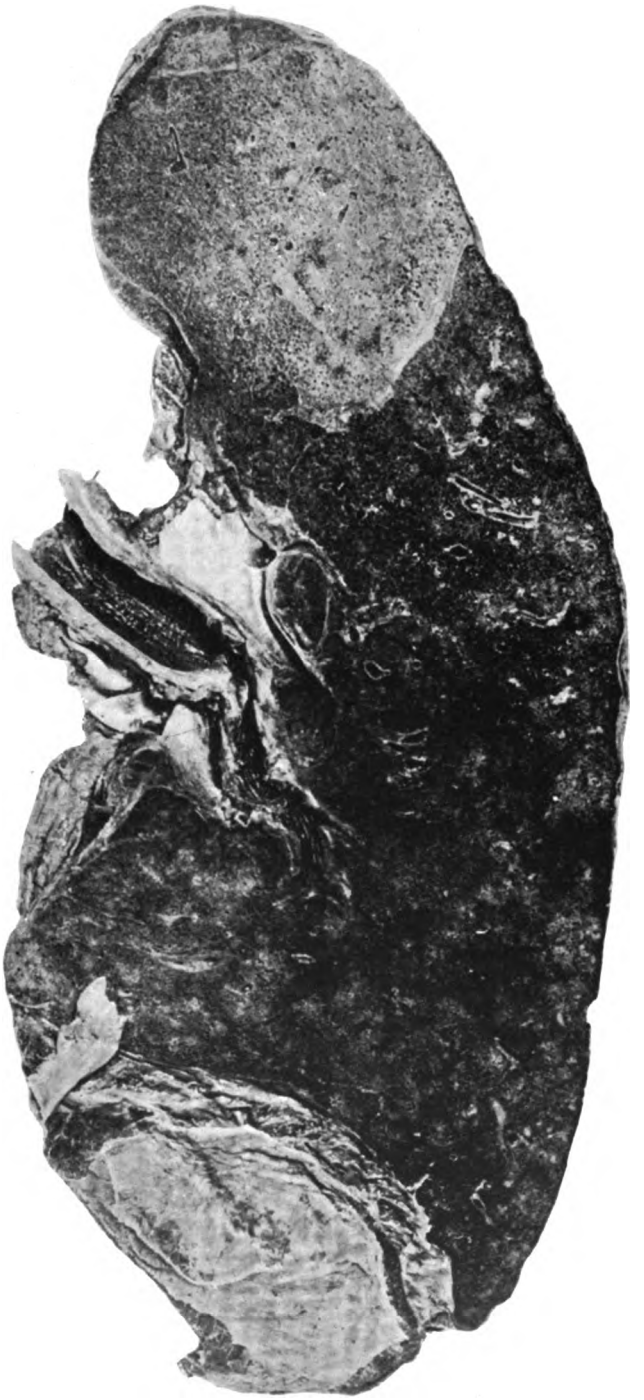

FIG. 44.

(MacCallum: Pneumonia in army camps.)

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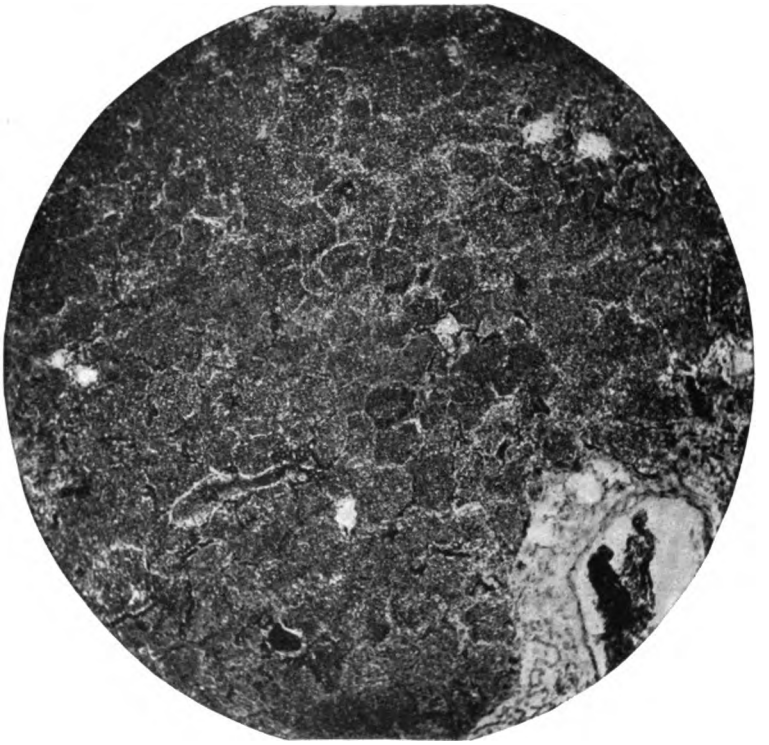

FIG. 45.

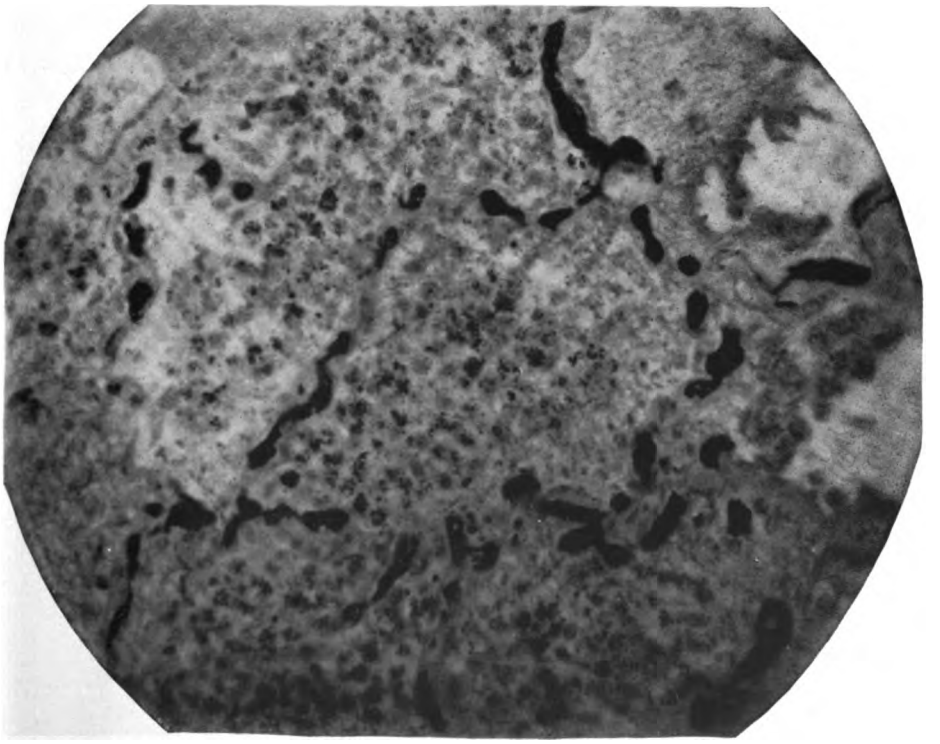

FIG. 46.

(MacCallum: Pneumonia in army camps.)

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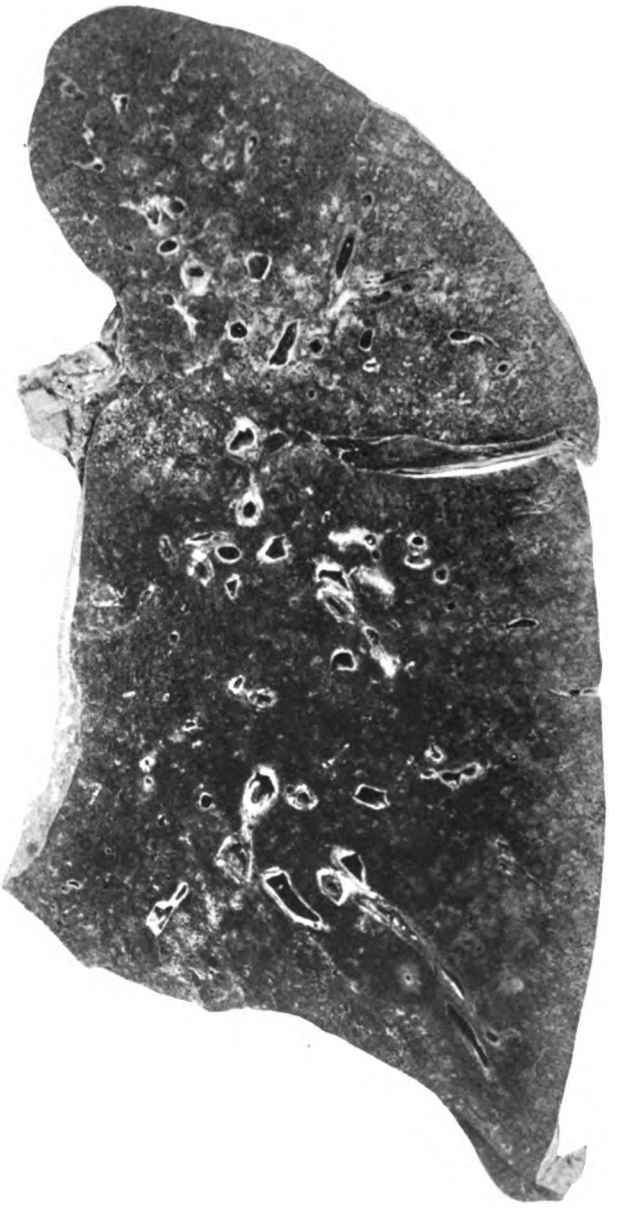

FIG. 47.

(MacCallum: Pneumonia in army camps.)

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FIG. 48.

(MacCallum: Pneumonia in army camps.)

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FIG. 48.

(MacCallum: Pneumonia in army camps.)

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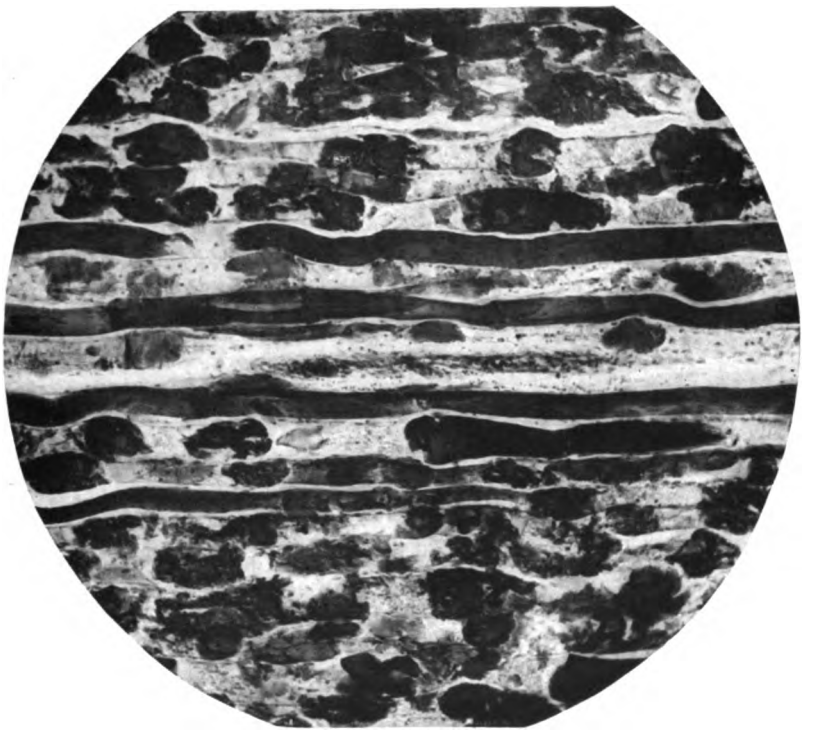

FIG. 49.

(MacCallum: Pneumonia in army camps.)

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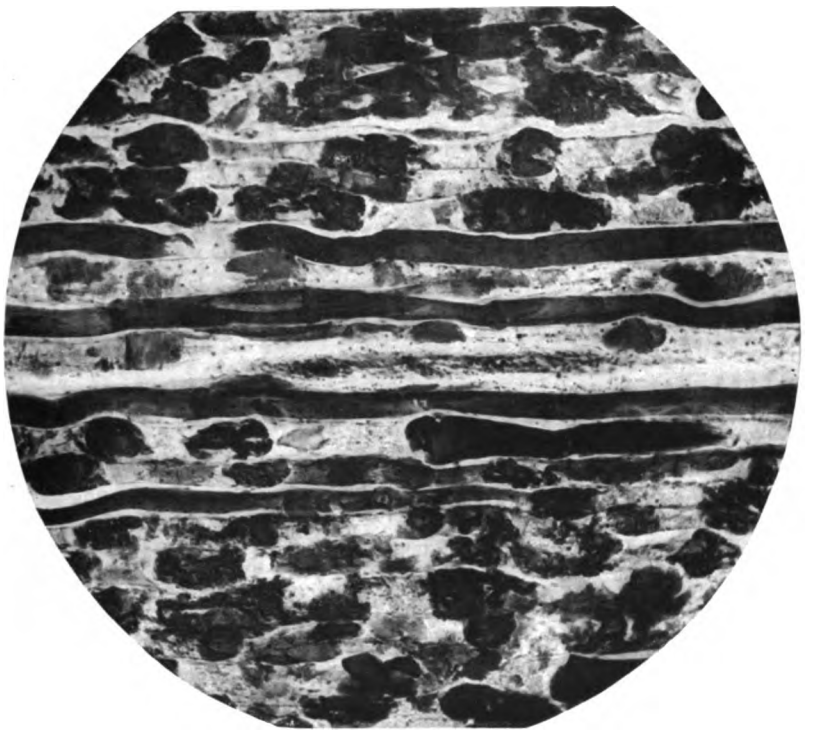

FIG. 49.

(MacCallum: Pneumonia in army camps.)

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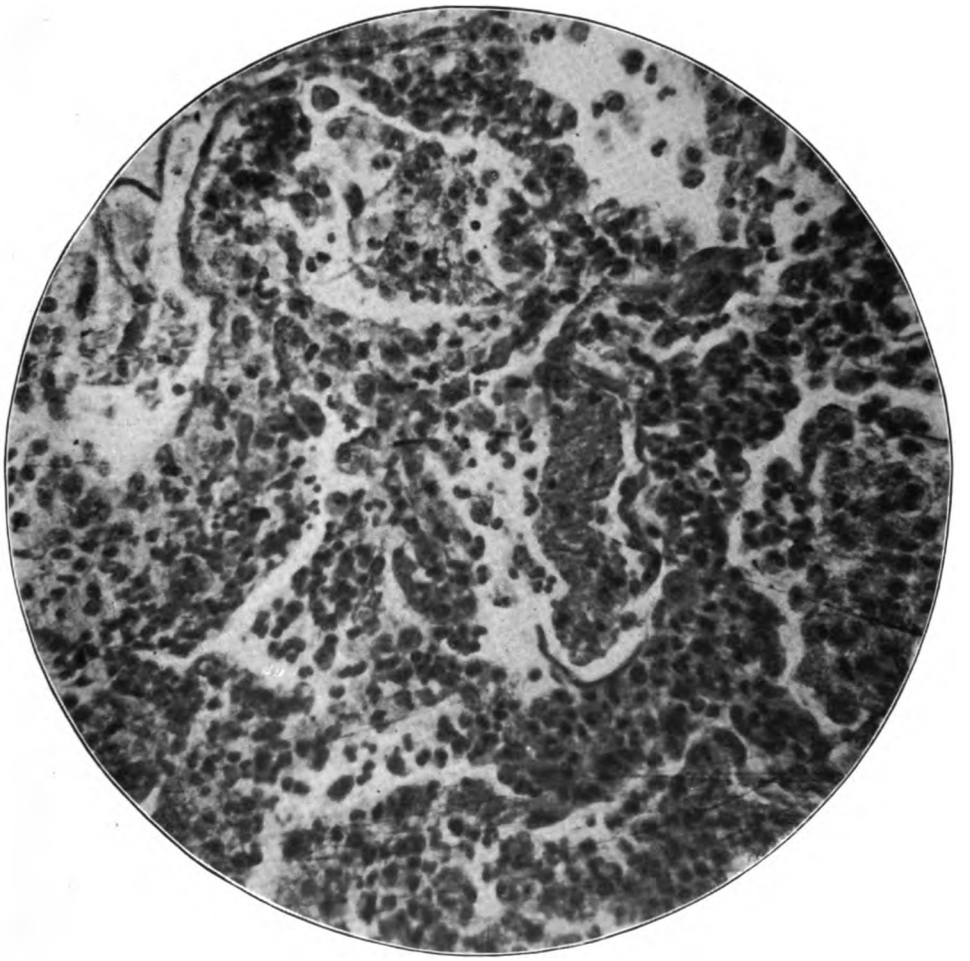

FIG. 50.

(MacCallum: Pneumonia in army camps.)

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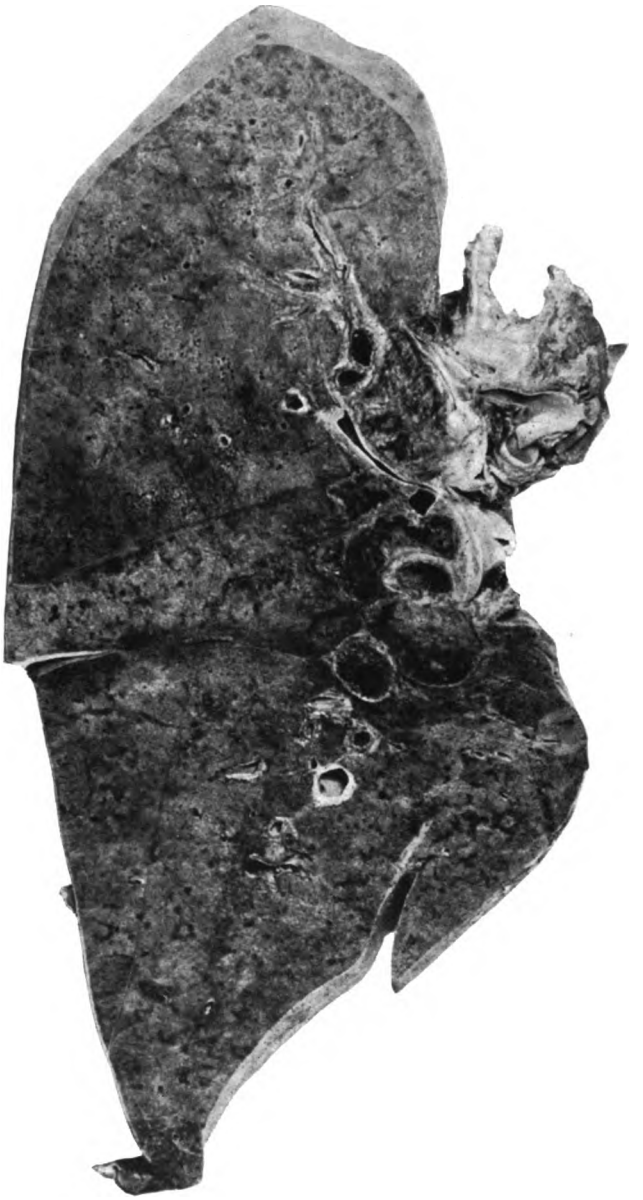

FIG. 51.

(MacCallum: Pneumonia in army camps.)

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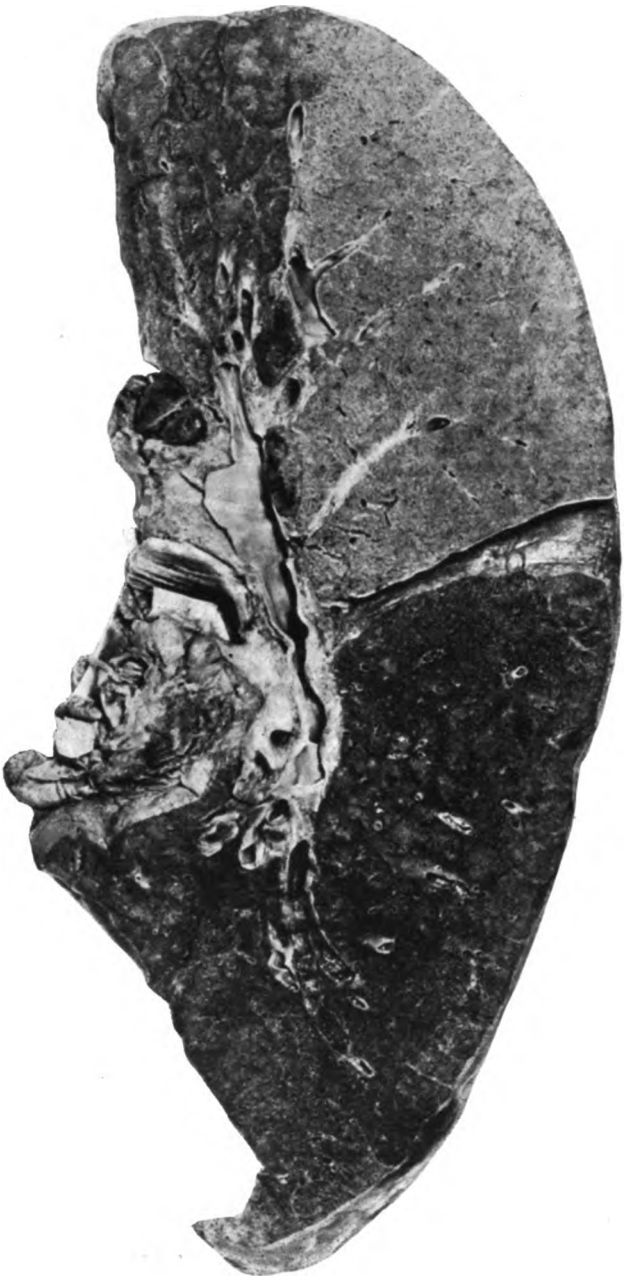

FIG. 52.

(MacCallum: Pneumonia in army camps.)

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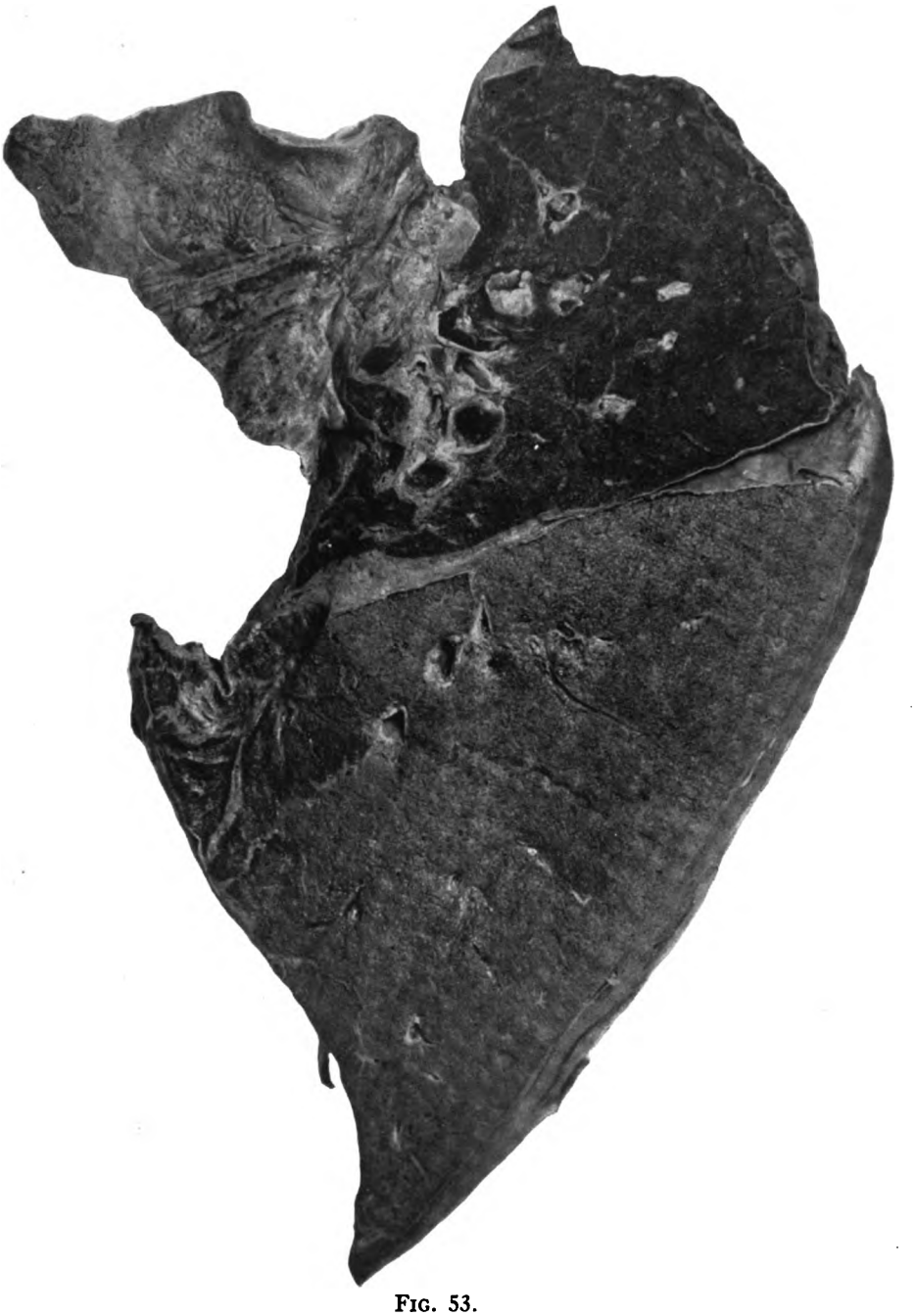

FIG. 53.

(MacCallum: Pneumonia in army camps.)

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FIG. 54.

(MacCallum: Pneumonia in army camps.)

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FIG. 55.

(MacCallum: Pneumonia in army camps.)

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PATHOLOGICAL ANATOMY OF PNEUMONIA ASSOCIATED WITH INFLUENZA

By W. G. MacCALLUM, M. D.

(From the Department of Pathology, The Johns Hopkins University, Baltimore)

The results of the study of the pathological changes in persons dying during the epidemic of influenza of the autumn of 1918, made by a commission sent to two army camps by the Surgeon General of the United States Army, were published in summary in March, 1919.

The opinions expressed in that paper have undergone no change as a result of further and more minute study of those cases and of others, and the present communication is designed mainly to put on record the details of the pathological anatomy of the respiratory organs in about 46 cases which formed the basis for those conclusions.

The material studied was derived from 20 autopsies at Camp Lee, Virginia, when the epidemic was nearing its height, and 12 at Camp Dix, New Jersey, made at a time when the influenza was practically over but when many cases of pneumonia were still in the hospital. Between these visits and afterward a number of autopsies were performed at The Johns Hopkins Hospital upon patients who died there in the early part of the epidemic. During the next winter—in January and February of 1920—there was, as is well known, a fresh outbreak of the disease and the tissues from several persons dying in The Johns Hopkins Hospital at that time were studied for comparison. Cases 213-230 were from Camp Lee; 80-91 from Camp Dix; 5113-6150 from The Johns Hopkins Hospital.

In all cases cultures were made from the respiratory tract as carefully as possible,* and the bacteria studied in smears and later in their relation to the lesions in sections. It is true that the methods of cultivating the influenza bacillus were greatly improved by Dr. Rivers after the first epidemic was over but this organism was quite

* The cultures were made at Camps Lee and Dix by Major R. A. Kinsella, at The Johns Hopkins Hospital by Drs. Bayne-Jones, Bollinger, Cross and others.

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successfully grown in practically all the cases in which it could be found in smears or in sections, and we feel no doubt as to its actual absence from cases in which it could not be found by any of these methods.

Tissues were fixed in Zenker formol in all cases and many large sections were made extending from the pleura to a point deep enough in the lung to include a rather large bronchus, and wide enough to contain two or more interlobular septa. In addition to hæmatoxylin and eosin, these sections were stained with various modifications of the Romanowsky stain, Giemsa, Wright, Wilson and others, these stains giving much information with regard to the types of wandering cells in the exudate. The combination Goodpasture-Weigert stain, described in a previous paper, was the other very useful one, since it distinguished Gram-positive and Gram-negative bacteria in relation to the lesion and colored not only fibrin but various granules. If this were preceded by a light stain with Weigert's hæmatoxylin, the result was a most beautiful preparation showing many histological details as well as the bacteria. Drawings in black and white were most easily made from sections stained with iron hæmatoxylin followed by Weigert's fibrin stain alone since there were no shades of red to be translated into terms of gray.

In the paper mentioned above it was pointed out that even yet we really have no idea of the nature of the living cause of the epidemic disease influenza and that all the bacteria found in the upper respiratory tract and lungs are to be regarded as secondary invaders. This is proven by the great inconstancy of all the organisms to which the rôle of causative agent has been ascribed. The influenza bacillus which, on account of the name gratuitously conferred upon it by Pfeiffer, quite naturally assumed first place in this discussion, did so because those who had the first opportunity of studying the disease happened to be working in a camp in which it was common. Few had the opportunity of observing the bacterial flora in cases in widely separated regions in succession, but those must have recognized the fact that although the character of the primary disease remained identical in all places, the bacterial invaders varied.

Thus, in Camp Lee we found practically no influenza bacilli and most of the cases showed Pneumococcus Type IV without other organisms. In only three cases were influenza bacilli found, whereas in Camp Dix, on the contrary, influenza bacilli were found in every case. At The

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Johns Hopkins Hospital influenza bacilli were rarely found. This conclusion was reached not only from the study of culture and smears but from the most minute survey of the stained sections, in which any considerable number of influenza bacilli could not be overlooked. It is supported to a great extent by the peculiarities of the lesions when influenza bacilli are actually present.

It would appear, therefore, that the organisms actually found as the causative agents of the pneumonia are greatly favored in their invasion and in their abundant multiplication by the extreme lowering of resistance to any infection, produced by the epidemic influenza itself. Since a great many different bacteria have been found producing pneumonia, often in complex mixtures, it would require very special evidence to prove that one of these is the universal cause of the primary disease. And since this particular organism is by no means always present it seems that the evidence is very weak.

Indeed, it appears probable that some other form of living virus not recognizable by our microscopic methods of staining, and not to be isolated or cultivated by methods at present in use, must be the cause of the epidemic. Further, it appears that the bacteria which are found must be fortuitous invaders, either because in a given community they have long been present without producing disease or because, having been introduced by a carrier, they spread rapidly to produce an epidemic in a crowded ward or barrack. The first of these is perhaps the best explanation of the frequent production of pneumonia by Pneumococcus Type IV, the second will explain the occurrence of pneumonias due to the hæmolytic streptococcus, other types of pneumococcus, or even the influenza bacillus. Such a local epidemic of staphylococcus pneumonia as described by Chickering is almost surely of this character.

Under these circumstances bacteria, present in the throat or introduced from without, readily invade the tissues of the whole respiratory tract and give rise to pneumonia. Because of the lack of resistance they multiply until they are present in such enormous numbers as are never seen under ordinary conditions. Although the predominant secondary infection appears to determine the anatomical character of the lesion there may be other successive infections with different organisms, so that it is often difficult to say which is the secondary and which the tertiary or quaternary infection. It seems possible that one or more of these bacteria may be present without producing any

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recognizable lesion whereas another produces pneumonia, or they may produce local modifications of the pneumonia such as areas of necrosis which involve tissue and exudate.

Nevertheless, we have gained the impression that in each instance there is a predominant organism which, if given time, establishes a recognizable type of pneumonia. There is no question as to the uniformity of the type of pneumonic lesion produced by the hæmolytic streptococcus, nor is there any doubt in our minds as to the character of that due to the influenza bacillus of Pfeiffer. Even the various types of pneumococcus which are so frequently predominant produce in time a form of lesion which is fairly specific although it must be admitted that it is not so easy to draw a precise and unmistakable picture of this.

There is a group of cases, made up of those which have run a short course and have led to a fatal issue in a few days after the onset of the influenza, in which the dilatation of the ductuli with hyaline lining and very fresh exudate is found.

In these we have found either the pneumococcus, sometimes in large numbers, or else very few organisms of any kind. These changes seem to be consistent with the presence of the pneumococcus even in great numbers but in all the other cases in which they are evident very few bacteria can be found in the sections or in smears. These may be staphylococci or mixtures of staphylococci and the influenza bacillus, Gram-negative cocci or even the hæmolytic streptococcus, but their numbers are so insignificant that it is difficult to believe that they have had full opportunity to develop their effects. Other cases of no longer duration, in which, however, the pneumococcal infection is much more intense, show no trace of this peculiar lesion of the ductules but a consolidation of a much denser sort with exudate which is advancing toward disintegration of the cells. Still more distinctive are the cases in which the hæmolytic streptococcus is the predominant or sole bacterium present. In these, as in the last group of our series, those in which the influenza bacillus of Pfeiffer occurs alone or in conjunction with other bacteria, the anatomical changes are very specific and quite characteristic, and the lesions of the ductules, if they ever existed, are entirely masked and obliterated.

With these points in view we may describe the cases in the following groups:

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1. Cases terminating fatally after a brief course in which characteristic dilatation of the ductuli alveolares with hyaline lining deposit is conspicuous. In some of these abundant pneumococci are present; in the rest, various bacteria in very small numbers.

2. Cases terminating fatally with great numbers of pneumococci in the lung and elsewhere and with a diffuse pneumonic consolidation in which the peculiar changes in the ductuli are masked or absent.

3. Cases in which a peculiar and characteristic pulmonary lesion is due to an overwhelming infection with the streptococcus hæmolyticus.

4. Cases in which *Bacillus influenzæ* is predominant or in pure culture. These seem to fall into two groups in one of which acute peribronchial infiltration is accompanied by extensive hæmorrhage and œdema, while in the other the slow course leads to the production of hard, nodular, peribronchial interstitial infiltrations of the tissue and exudation into the alveoli and bronchi.

GROUP 1.—*Fresh pneumonia with widened ductuli alveolares and hyaline lining layer; œdema and hæmorrhage.*

A. Predominant pneumococcus—
212, 218, 221, 223, 224, 82, 5713, 5714, 5722, 5726.

B. Staphylococcus infection—
211, 6143.

C. Streptococcus infection (questionable and slight)—
5706.

D. Gram-negative cocci (Meningococci or M. catarrhalis)—
83, 226.

CASE 212.—D. D. Taken sick September 17, 1918, with headache and backache, was admitted September 23 with a temperature of 105° F., pulse 120, resp. 30. Dyspnœa, cyanosis, signs of pulmonary consolidation, delirium and death on September 26. Autopsy September 27, 17 hours later.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia. Bilateral fibrinopurulent pleurisy. Acute splenic tumor. Hyperplasia of bone marrow.

Slight jaundice and cyanosis. The *left pleural cavity* is largely obliterated by fresh fibrin which glues the surfaces together not only externally but between the lobes. A few cubic centimeters of turbid fluid are held in the meshes of the fibrin. The *right pleural cavity* is also obliterated by the gluing together of all opposed surfaces with a thin layer of fresh fibrin. The cavity contains about 100 c. c. of turbid fluid. Mediastinal tissues are infiltrated with yellow fluid and the retrosternal lymph glands are enlarged.

The whole posterior surface of the *left lung* is covered with a thick honeycomb-like yellow exudate. The more anterior parts of the lung are

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air containing but in the posterior part of the upper lobe there is a large mass of consolidated tissue measuring about 6 cm. in diameter. This has evidently been formed by the confluence of lobular areas of consolidation since interlobular septa form its outline in places. It is sharply elevated above the surrounding air-containing lung and shows a granular surface. It is surrounded by a softer hæmorrhagic zone and has occasional patches of hæmorrhage in its central part. Bronchi, blood vessels, interlobular septa and lymphatics are not conspicuously altered. In the lower lobe there are several similar areas with surrounding hæmorrhage.

The *right lung*, covered as in the case of the left with thick fibrin, shows a large firm area of consolidation which occupies all the more anterior portion and which on section proves to be about 5 cm. in diameter and uniformly solid except for some purplish sunken patches of collapse. The outer and anterior portion of the lower lobe is consolidated in the same way. As in the left lung there is no change in the framework nor in the bronchial walls. They are reddened and the lining is smeared with an opaque brownish frothy mucus.

Cultures from both lungs, heart's blood and pericardium show Pneumococcus Type I. That from the spleen was negative. There were no influenza bacilli in cultures or in smears from the lung.

Microscopical Examination.—The lung shows a fresh but rather dense pleural exudate overlying the intact pleural lining cells. The interlobular septa are œdematous and infiltrated with leucocytes and some red corpuscles. The lymphatics are filled with leucocytes but not greatly distended. The bronchi contain a few leucocytes but everywhere their epithelial lining is intact. Different degrees of consolidation occur. There are patches in the more central part of the large area in which the alveoli are most densely packed with an exudate in which the leucocytes are almost all disintegrated and the blood corpuscles faded. In these areas, however, the alveolar walls are never necrotic but contain circulating blood. Other areas show a far fresher consolidation with much œdema and hæmorrhage. In these the ductuli alveolares are distended with fluid and lined with the hyaline fibrinoid material so often described. The alveoli contain a loose exudate with much fibrin, well preserved blood and polymorphonuclear leucocytes and in places huge numbers of pneumococci in pairs and short stiff chains. No influenza bacilli are seen, nor are any other organisms found.

Case 218.—T. S. Began September 6, 1918, with frontal headache and drowsiness, later fever with chilly feeling. Slight cough. No general pains or epistaxis. Entered hospital September 22 with temperature 103.3°, pulse 96, resp. 24. General pains, chills, fever and cough with blood-stained expectoration. No history of physical examination but patient died September 29 at 8.25 a. m. Autopsy three hours after death.

Blood Count.—	Leucocytes	Differential count Polym.	S. M.	L. M.
September 23.....	7150	66	28	6
September 26.....	6400	76	22	2

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Anatomical Diagnosis.—Bilateral confluent lobular pneumonia.

The *left pleural cavity* contains about 20 c. c. of fluid. Surfaces are glistening but roughened in places, especially over the middle of the anterior edge of the upper lobe and on the mesial surface. The diaphragmatic surface is smooth.

The *right pleural cavity* contains about 20 c. c. of fluid. The surfaces are everywhere glistening but are much discolored in places by opaque red patches which seem to overlie the prominent nodules in the lung. The interlobular septa in the middle lobe are emphysematous. In the anterior portion the consolidated lobules contrast sharply with those which are air-containing.

The *left lung* is very large and heavy. The upper lobe is mottled with alternating consolidated and air-containing lobules or groups of lobules. The largest mass of these consolidated lobules lies in the posterior lower part and spreads out fanwise toward the anterior margin where the pleura is covered with an opaque yellow layer of fibrin. On section these areas are dark greyish purple with patches of pale greyish white in which it is evident that, although plugs of exudate project from the alveoli, except for these the cut surface is smooth although the consolidated areas are elevated above the air-containing portions. The bronchi, blood vessels and interlobular septa are not especially altered. In the lower lobe the upper posterior part is firm, airless, dark purple and studded here and there with white patches, but it is elastic and not rigid or hard. Section shows numerous scattered patches of consolidation which in the centre are generally grey in contrast with the darker red consolidated marginal part. These too show clusters of small whitish areas. The fluid which exudes from the surface is glutinous. The lower and anterior parts of the lobe are air-containing.

The *right lung* (Fig. 1) is very large. Its upper lobe is studded even to the anterior margins with groups of lobules which are firm in contrast with the intervening air-containing lobules. The posterior part is almost entirely solid. The middle lobe shows some interstitial emphysema and contains scattered groups of consolidated nodules. The lower lobe is almost entirely solid posteriorly but contains air near the anterior margin.

On section through the lung it is found that the upper lobe is occupied by whole consolidated lobules which are sometimes grey with distinct alveolar plugs of exudate, sometimes dark greyish red, firm and elastic but with a smooth cut surface. The middle lobe shows scattered patches of the purplish elastic type of consolidation. In the lower lobe the entire upper and posterior part is consolidated, the dense tissue being greyish red, elastic and firm with only the most indefinite alveolar plugs, although in certain lobules minute yellow plugs project. Throughout the whole lower portion there are confluent, deep greyish purple, elastic areas from which there project smaller dense, irregularly outlined, rough, greyish yellow patches in which the opacity of the alveolar exudate is much greater. The bronchi are not particularly reddened and the framework of the lung is not abnormal. The most striking feature consists in the presence of these groups of opaque yellowish brown areas merging into

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pale, almost white patches scattered in the more elastic confluent areas of consolidation. But another feature which is remarkable arises from the fact that on standing a thick grey, glutinous cloud of fluid emerges from each alveolus or terminal bronchiole so that the cut surface is quickly covered with a layer of sticky fluid which may be lifted up into long strings.

The other organs are normal in appearance.

Cultures at autopsy showed Pneumococcus IV from lungs, pleura, heart's blood and spleen. Some colonies of a hæmolytic staphylococcus were also found in the lungs.

Microscopical Examination.—Sections from the two lungs show essentially similar changes. The pleura is thinly covered with a corrugated layer of dense fibrin. Its tissues are spread apart by an accumulation of exudate so that the layer upon which the pleural lining cells lie is widely separated from a perfectly uniform underlying membrane which appears to be composed of elastic tissue. The exudate consists chiefly of coagulated fluid with a few leucocytes and red corpuscles, but it is heavily loaded with pneumococci which lie free in the delicate meshes of fibrin. The interlobular septa are in some places much more changed than was suspected from the examination of the gross specimen. They are broadened by an accumulation of exudate consisting of fluid, fibrin, wandering cells and great quantities of pneumococci. The lymphatics are in places distended with a thrombus containing bacteria. The bronchial walls are rarely infiltrated with cells, although they have lost most of their epithelium and are filled with coagulated fluid and leucocytes. The terminal bronchioles are distended with fluid and cells. Their epithelium soon disappears but is for a time overlaid by a thick layer of hyaline material probably of fibrinous origin, although it fails to give the staining reaction for fibrin. This hyaline layer is particularly thick and conspicuous in this lung and extends to line the ductules and even to enter the air cells. Some of the latter are full of a similar dense pink-staining material. In general the alveoli in every section are greatly dilated and, except in the opaque areas described above, are rather loosely filled with leucocytes. In places the leucocytes are clumped together in the center and the remaining space is occupied by a thick fluid. Indeed there are some areas in which the alveoli contain nothing but fluid which has been coagulated by the fixing fluid into a crumbly pink-staining material. It is, however, loaded with free pneumococci, most often in pairs but sometimes in short chains. Very few of them are enclosed in leucocytes.

There are other areas, however, in which the alveoli are widely distended by a dense exudate of leucocytes, mononuclear cells and desquamated epithelium all entangled in a close network of fibrin. This exudate also contains numerous pneumococci. The cells are in many alveoli almost completely disintegrated and form a dust of nuclear fragments. There are not many red corpuscles. Indeed hæmorrhage is scarcely a prominent feature of the consolidation. The alveolar walls are thin, in part injected with blood but in places traversed by capillaries in which hyaline thrombi,

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probably formed from agglutinated corpuscles, block the canal. In places they are actually broken through without any evidence of hæmorrhage.

No organisms other than the pneumococci are found but these, as is especially well shown in smears made from the fresh lung, are surrounded by exceptionally thick capsules. No bacilli either Gram-negative or Gram-positive could be found and most careful search failed to reveal any organisms resembling influenza bacilli.

The other organs show no especial abnormality.

CASE 221.—F. B. Entered hospital at Camp Lee on September 26, delirious and with signs of consolidation in the lower right lobe. No further history except that his illness began on September 19 with aching and general malaise. Temp. 103-106.4°. Pulse 102-120. Respirations 28-66. Died September 30, 1919. Autopsy 6 hours after death.

Anatomical Diagnosis.—Bilateral confluent bronchopneumonia; ulcerative laryngitis.

The *left pleural cavity* contains very little turbid fluid; the surface is smooth but shows scattered areas of brick-red staining.

The *right pleural cavity* contains about 50 c. c. of turbid fluid. Its surfaces are smooth but stained over the consolidated areas a brick-red color.

The *left lung* is very large and is air-containing in the upper and anterior parts of the upper lobe and in the anterior part of the lower lobe. The rest is firm, elastic, rather flabby and airless. The whole mesial surface of both lobes is air-containing and the solid area occupies practically the whole posterior part of the lobes. The bronchial glands are somewhat enlarged. On section the consolidated area in both lobes is not quite homogeneous but is in general dark greyish red in color. The cut surface is spongy and exudes a quantity of bloody fluid. The spongy appearance is seen to be due largely to the widening of the terminal bronchioles and ductuli alveolares which become visible as minute cavities separated by zones of true alveolar tissue which is of fine texture. In most of the confluent areas of consolidation there are no distinct plugs of exudate but these minute cavities contain fluid which is easily squeezed out after which the spaces draw themselves open without any appreciable contents. There are, however, a few more prominent areas of consolidation which are firmer and in which distinct plugs of exudate are visible.

The *right lung* is very voluminous. The upper and anterior part of the upper lobe and the anterior parts of the middle and lower lobes are air-containing and there is an interstitial emphysema in this portion of the upper lobes. The posterior and lower part of the upper lobe is elastic, partly crepitant, not very firm. The whole posterior part of the lower lobe is heavy, fairly firm and elastic, not rigid.

On incision a great quantity of blood-stained fluid pours out. The consolidation in the upper lobe is patchy with a great deal of intervening air-containing lung. In the lower lobe the consolidation is uniform and has the same coarse spongy character without distinct alveolar plugs of exudate as seen in the left lung.

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Organs of the Neck.—Tonsils somewhat swollen especially the right one. Tongue, epiglottis and pharynx pale and normal. Larynx and vocal cords normal except for a small grey patch at the base of the epiglottis and a similar patch a short distance below the vocal cords on the left side.

Nasal Sinuses.—The sphenoid sinus contains a gelatinous fluid which readily escapes when the membrane is punctured. The lining is not hyperæmic but practically normal in appearance. The frontal and ethmoid sinuses are normal. The middle ear and mastoid cells are also normal.

Cultures from the lungs developed many colonies of Pneumococcus Type IV, together with a staphylococcus. Those from the left pleura, heart's blood and spleen were sterile. That from the frontal sinus showed the same pneumococcus while the sphenoid sinus contained a gram-negative bacillus.

Microscopical Examination.—The lungs show in all the sections a very fresh pneumonic consolidation which is dense in some areas but around their margins fades away into a slight hæmorrhagic œdema. In this fluid bacteria are still abundant. The pleura is in places infiltrated with blood corpuscles and evidently stained with hæmoglobin. There are no great numbers of bacteria there. The interlobular septa are somewhat widened and œdematous. The lymphatics both there and in the walls of the bronchi and the blood vessels are dilated and filled with fluid and a delicate network of fibrin. The bronchi contain chiefly fluid with few cells. Their walls are not thickened or infiltrated. The alveolar walls are not especially thickened or infiltrated with cells, but the capillaries are widely distended with blood. The ductuli alveolares are very much dilated and contain fluid with a delicate network of fibrin and a relatively small amount of cellular exudate. Their walls are lined with a homogeneous layer of material which stains red with eosin and gives an indistinct purple stain with the gentian violet used in Weigert's fibrin stain. This hyaline material is therefore not precisely identical with fibrin; it extends so as to line many of the alveoli.

In the alveoli themselves the epithelial cells are swollen and often desquamated. They are not especially pigmented. On the other hand, there are many large mononuclear pigmented cells in the alveolar cavities and these are to be found also in the interstices of the tissue of the lung. The alveolar exudate is composed largely of red corpuscles which are well preserved. In places the cavities are packed with them, but elsewhere the alveoli contain a great deal of fluid. There is a delicate network of fibrin throughout. Polymorphonuclear leucocytes form another prominent element of the exudate but they are not really very numerous. There are, however, many mononuclear cells most of which are not quite as large as the leucocytes and have a very deeply stained, small round nucleus and a protoplasm which is slightly granular and takes a rather deep eosin stain. There are other larger cells with a single vesicular nucleus and faintly stained cell substance. There is no evidence of disintegration of the cells and no sign of organization so that the process appears very fresh. Smears

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from the lung showed only pneumococci. In section these are the predominant organisms. They are fairly abundant especially in the more œdematous part of the area of consolidation, but they are not so numerous as in some other cases. No other organisms are seen in any great numbers, but there are occasionally found clumps of Gram-positive cocci which look like staphylococci. In three alveoli after long and diligent search there were found twisted strands of rather large Gram-negative bacilli. None of these were intra-cellular and they seem too large to be regarded as influenza bacilli.

The other organs show the following changes in so far as they present any abnormality.

The bronchial lymph glands have their sinuses packed with mononuclear cells together with pneumococci. The lining of the sphenoid sinus shows œdema and hæmorrhage with much leucocyte infiltration, the lumen is full of a mucopurulent exudate loaded with Gram-positive cocci, apparently pneumococci. There are no influenza bacilli.

The larynx shows a diphtheritic inflammation with pneumococci scattered in the tissue and exudate but with no bacilli. The trachea shows some pneumococci and many very large bacilli which stain irregularly. No influenza bacilli.

The rectus abdominis muscle presents extensive fresh hyaline degeneration.

CASE 223.—H. C. Had been sick since September 11, 1918. Onset with chill, general aching, headache, nausea and vomiting. Began to cough September 23. Was brought to hospital September 26 with impaired vocal fremitus at the base of the left lung. No further history. Died September 30. Autopsy 13 hours after death.

Anatomical Diagnosis.—Bilateral lobular pneumonia; Hyaline degeneration and rupture of rectus abdominis muscle with hæmorrhage.

The right rectus abdominis muscle seems normal, but the left is ruptured transversely in the lower third and in the intervening space there is an extensive hæmorrhage.

The *left pleural cavity* contains about 20 c. c. of dark brown fluid; surfaces smooth and glistening.

The *right pleural cavity* contains 50 c. c. of dark brown turbid fluid. The surfaces are slightly roughened, and over the lower lobe there are several patches made up of small opaque greyish brown elevations, as well as other patches of dark red-paint-like material.

Left Lung.—The upper lobe contains air except in certain firm areas which project from the posterior lower part. The lower lobe similarly presents nodules varying from 1 cm. to 5 cm. in diameter which project, but otherwise it seems to be air-containing. On section these areas in the upper lobe are dark brown, almost black or slate color; they are not much elevated, not very firm, sharply outlined by their color and by their increased resistance. They do not present any definite alveolar plugs. In the lower lobe the same condition is noted where there are numerous

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scattered brownish or blackish patches, indistinctly outlined and not very firm. In the posterior portion of the lower lobe the consolidation becomes more confluent. The area is not firm, exudes a great quantity of brownish fluid, and contains no definite alveolar plugs.

Right lung.—The upper lobe shows a rather spongy consolidation in the uppermost part posteriorly. Otherwise it is air-containing. This spongy area is greyish red superficially. The middle lobe is similarly consolidated in the posterior part. The consolidation is a little firmer and shows distinct alveolar plugs. The anterior part is air-containing. The lower lobe is almost entirely consolidated. The cut surface shows a fairly firm, spongy dark red tissue in which alveolar plugs are not really distinct. The ductuli appear to contain only fluid but their walls seem thickened. A great deal of bloody fluid oozes from the lung. The lymph glands are much enlarged at the hilum, and deep into the substance of the lung.

Organs of the Neck.—The uvula, pharynx, tongue and tonsils seem normal. The epiglottis and vocal cords are normal. The larynx is rather pale but the trachea below the larynx is deep red in color.

The other organs show no special abnormality. The *bonemarrow* is almost entirely fatty.

Cultures from both lungs, the right pleura, pericardium, heart's blood, and from the ruptured rectus abdominis show Pneumococcus Type IV. The plate from the left lung contained also a staphylococcus. That from the right lung a coarse Gram-positive bacillus.

Microscopical Examination.—Sections through various parts of the lung show dense areas of consolidation, in some places with much hæmorrhage, and in other areas a very fresh exudate which is rather loose and fails to fill the alveoli solidly. In these areas the ductuli alveolares and the atria are in many places lined with a hyaline material (Fig. 2).

Closer examination shows that in the areas of denser consolidation the capillaries are only in part open and conducting streaming blood. There are in many short stretches of the alveolar wall no blood corpuscles, instead the capillaries are plugged with an indefinite mass which only occasionally gives the fibrin stain, but from which many distorted leucocytes are seen to be wandering out into the alveolus.

In the less densely consolidated part, and indeed everywhere, the epithelial lining of the alveoli seems practically completely desquamated. The underlying structureless membrane is lifted high off the capillaries on each side by fluid and leucocytes. The hyaline material which does not stain by Gram's stain, but which in places seems to show included red corpuscles, is formed in close apposition with this membrane. It does not replace the epithelium; where that is still present it overlies the hyaline substance. The alveoli are full of leucocytes which are packed with pneumococci.

The pleura is loaded with organisms but there is no fibrinous exudate on its surface. The grayish brown patches are found to be areas of œdema crowded with bacteria; apparently it is the actual mass of bacteria that

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gives the peculiar dull color. The interlobular septa are, as a rule, spread apart by accumulations of an exudate of fluid, fibrin and leucocytes with a great many bacteria.

CASE 224.—S. P. Taken sick September 21, 1918, with general soreness, chills, cough and expectoration of blood. On admission, September 28, there was no consolidation, but there were mucous râles and some slight dullness. Throat inflamed. No further history. Died September 30. Autopsy 9 hours after death.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia.

Rectus muscles apparently normal.

The *left pleural cavity* contains a little brownish fluid; surfaces smooth and glistening.

The *right pleural cavity* contains about 30 c. c. of brownish fluid; surfaces smooth and glistening.

Left Lung.—The upper lobe is air-containing except for a mass at about its middle. The lower lobe is practically entirely solid except for the upper posterior angle. It is elastic, rather œdematous, and pits on pressure. On section the upper lobe is largely air-containing, but in its middle portion shows a firm area which is slightly elevated, smooth and moist, exuding a clear fluid and blood. It is grayish red without any definite alveolar plugs. The lower lobe is much more extensively consolidated, but it too on section is smooth, moist, exudes a grayish fluid and is nowhere roughened by projecting plugs with the exception perhaps of two or three small groups of alveoli.

The *right lung* (Fig. 3) is voluminous, heavy, pits on pressure over the whole posterior part of the upper lobe, all but the upper part of the middle lobe, and all but the anterior lower margin of the lower lobe. Over the lower lobe near its lower margin, there are some yellowish white elevations, pinhead in size, scattered in the pleura. These are accompanied by the dull red stains so frequently noted. The lung on section exudes a brownish fluid. The bronchial glands are large and pigmented. The upper lobe is found on section to be partly air-containing. The rest is firm, smooth moist, and greyish red without showing any definite plugs of exudate. The lower lobe shows a smooth grayish red cut surface upon which it is difficult to outline exactly the consolidated part, but there are a few patches which are rather more elevated and darker. There is in this lung, more than in any of the preceding, the peculiar springy elasticity and gelatinous moist surface, with little evidence of dry alveolar plugs, characteristic of a very fresh consolidation. The same condition prevails in the middle lobe. The tongue, tonsils and pharynx are normal. The glottis is slightly œdematous. The vocal cords are normal, but the mucosa of the larynx and trachea is somewhat reddened.

Cultures from the right lung, right pleura, and heart's blood showed Pneumococcus IV in pure culture; those from the spleen and pericardium were negative. Smears from the lung show pneumococci with capsules but no other organisms. The influenza bacillus was especially searched for.

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Microscopical Examination.—Large sections taken through several lobules of the consolidated lung show a remarkably uniform early or fresh consolidation (Fig. 4), which in the section has a curious spongy appearance because of the dilatation of the ductuli alveolares which are distended with fluid and lined in part with the hyaline material already mentioned in other cases. There is only moderate œdema and spreading apart of the interlobular septa and other parts of the framework of the lung and the bronchi usually contain very little exudate. The smaller bronchioles have suffered some desquamation of their epithelium and in the ductuli all the more prominent points are thickly covered with the homogeneous eosin-staining hyaline material which seems to form upon, or in connection with, the thin structureless membrane which underlies the epithelium. The epithelium itself, if not entirely lost, is found adhering to the surface of this layer. The alveoli contain a delicate network of fibrin in the meshes of which lie relatively few cells, all of which are very well preserved (Fig. 5). Red corpuscles form a large proportion of these and sometimes fill groups of alveoli completely. There are many polymorphonuclear neutrophile leucocytes which are actively phagocytic and contain pneumococci, but there are also many free organisms. With the combined Goodpasture and Weigert stain it is found that the pneumococci are the only bacteria present and they are in small numbers as compared with the myriads found in some cases. In the phagocytic leucocytes there are almost as many mononuclear cells which fall into several groups. Of these there are first, certain small cells not much larger than red corpuscles with a deeply stained small round nucleus and sharply outlined cell body which with Giemsa's stain seems finely granular. Of these there are three or four in each alveolus. They are not evidently phagocytic, and are possibly to be regarded as lymphocytes, although the solidity of the nucleus and the green stain which it takes with methylene blue are not precisely characters of the lymphocyte. These are doubtless the cells described by Pratt in his studies of the early stages of lobar pneumonia. The larger mononuclear cells are more abundant and it becomes difficult to decide as to their exact nature. Some of them are directly traceable to such connections with the alveolar epithelium which still adheres so that there can be little doubt that they are desquamated epithelial cells. These are often phagocytic and some of them are swollen or bloated and no longer stain clearly or deeply. But there are many other large mononuclear cells which do not seem to be of this nature, partly because they can be found wandering in considerable numbers in the tissue of the lung and especially in such places as the walls of the bronchi and blood vessels. These are not morphologically very different from the desquamated epithelium but it seems probable that they belong to that series of mononuclear wandering cells derived from lymphocyte-like cells in the beginning and always abundant in the meshes of the tissues and ready to approach an area of infection. Their protoplasm stains rather deeply and has a finely granular appearance but one cannot stain any specific granules there even with the aid of Wilson's, Wright's or Giemsa's stain which readily bring out the neutrophile granules of the leucocytes.

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In the walls of the bronchi and elsewhere there are some mast cells the granules of which stain a brilliant deep wine color with the stains just named. In the alveolar walls most of the capillaries are seen to be normal and transmitting a stream of blood corpuscles, but in nearly every alveolus there are some of these capillary channels which are plugged with minute capillary thrombi which stretch across the wall of the alveolus. It is from these thrombosed portions of the capillaries that leucocytes are seen wandering out and caught by the fixing fluid in the act of stretching the cell body and nucleus through the alveolar wall.

CASE 82.—L. J. Began to feel ill on September 25, 1918. On October 4 he had a chill with headache, backache, cough and pain in chest. Admitted to hospital October 6. Bronchial breathing and moist râles over both lower lobes noticed on October 9. On October 10 dullness over both bases. Patient very sick with dyspnœa and cyanosis. Delirious. Temp. 103°. Pulse 88-136. Resp. 28-54. Urine negative. Leucocytes 8400. Polynuclears 84 per cent. S. M. 14. Transitionals 2. X-Ray examination shows a few scattered areas of consolidation. Death on October 11. Autopsy two hours after death.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia. Rupture of rectus abdominis with hæmorrhage.

Rectus Muscle.—The rectus abdominis on the right side shows an extensive hæmorrhage between the torn ends of the ruptured muscle. On the left side there are small ruptures of the pale musculature with hæmorrhage.

The *left pleura* contains about 100 c. c. of turbid grayish fluid. The surfaces are fairly smooth but over the posterior aspect there are confluent elevated patches of a pale grayish yellow color which, although only from one to two millimeters in diameter, are so numerous as to cover a large part of the pleura.

The *right pleura* is partly obliterated by adhesions, but also contains 350 c. c. of grayish brown fluid.

The *left lung* is very voluminous and heavy. Its upper lobe shows a perfect checkerboard of alternately purple and pale grayish pink lobules. There are also patches of deep red paint-like discolorations on the pleural surface. On section the upper part of the lobe, while in general air-containing, presents numerous airless, elastic dark red lobules which are firm but not rigid. The lower part of the lobe is not consolidated. These patches are more numerous anteriorly and stand up above the cut surface. They are coarse and spongy, very œdematous but without any definite plugs of exudate.

The lower lobe is almost entirely firm except in its anterior lower portion where it is checkered with patches of deep blue. On section it is very œdematous, almost entirely airless and presents several areas of consolidation which are prominent and outlined usually by interlobular septa. These are dark brownish red, very spongy, moist and elastic but not rigid. No plugs of exudate project but the cut surface exudes a bloody fluid. The bronchi are pale and contain a frothy brownish fluid.

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Right Lung.—The condition found in this lung is precisely that described for the left except that the consolidation is even more extensive (Fig. 6).

The tracheal mucosa is grayish pink and shows no ulceration. The tissue about the vocal cords is œdematous and the cords themselves and the mucosa just below them show a shallow ulceration.

Cultures.—From the heart's blood there was cultivated a pneumococcus. The lungs showed in smears and in cultures a pneumococcus which was associated with the micrococcus catarrhalis. Mice inoculated from each lung died with pneumococcus in the peritoneum and heart. Smears and cultures from the trachea gave Pfeiffer's influenza bacillus.

Microscopical Examination.—Some of the sections of the lung show a dense hæmorrhage in the substance of the pleura which corresponds with the paint-like discolorations described. In other places the pale coffee-colored elevations are found to correspond with masses of pneumococci in the œdematous pleural tissue. The areas of consolidation are of different density. Most typical are those in which the ductuli alveolares are enormously dilated with fluid, each projecting interalveolar septum being capped with a hyaline red-staining material which lines the ductulus, extends into the alveoli, and is thickest over the most prominent points. The fluid is practically cell-free but is full of minute bubbles about which pneumococci are clustered. The actual alveoli between these dilated ductuli are full of a fresh exudate of red corpuscles with leucocytes and a delicate network of fibrin. This exudate is fairly loaded with pneumococci.

The exudate in these alveoli is quite fresh and instead of being composed chiefly of polymorphonuclear leucocytes contains very many small cells not larger than a red corpuscle with single round, deeply stained nucleus and finely granular protoplasm (Fig. 7). These cells are characteristic of the earliest stages in the production of the exudate and have been described in other cases. Their exact nature is obscure.

Case 5713.—G. R. B. Age 31. Onset on September 27, 1918, with general malaise, sore throat, photophobia and severe headache. On October 1 he had a free epistaxis. Admitted to the hospital on October 4 with general tenderness over body, and signs and symptoms of bronchopneumonic consolidation especially in the lower lobes. Temperature 102-104.4°. Death October 6. Autopsy 12 hours after death.

Anatomical Diagnosis.—Confluent lobular pneumonia with fibrinous pleurisy.

The *left pleura* contains 20 c. c. of dark cloudy fluid. The surface is roughened posteriorly and on the diaphragmatic surface but is otherwise smooth.

The *right pleura* contains 10 c. c. of similar fluid. The surfaces are smooth and glistening.

The *left lung* is heavy and dark purplish red, especially in the posterior portion of the lower lobe where the surface is covered with a thin layer of fibrin. The upper lobe on section shows patchy areas of consolidation separated by air-containing tissue. The lower lobe is firm

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and almost completely consolidated, but there are some air-containing lobules. The cut surface is covered with grayish red fluid.

The *right lung* presents the same dark red color as the left. The lower lobe and the inferior third of the upper lobe are almost completely consolidated and the cut surface oozes a dark reddish fluid.

Trachea.—The trachea contains much turbid dark fluid. Its mucosa is congested and covered with a thin fibrinous exudate.

Cultures from the lung showed Streptococcus hæmolyticus and Staphylococcus aureus.

Microscopical Examination.—The pleural surface is not especially altered but the membrane itself is œdematous. The interlobular septa are very greatly widened by œdema and this is true to a less extent of the adventitial walls of the bronchi and blood-vessels. The lymphatics are not conspicuously dilated. The œdematous interlobular septa are sparsely infiltrated with mononuclear cells of various sizes and shapes, most of which are of the type of lymphocytes, but there are larger, more deeply stained cells and a few with distinct basophilic granules.

The bronchi show a moderate desquamation of the epithelium. They contain chiefly blood with a few mononuclear cells—both staphylococci and pneumococci are found there. The ductuli alveolares are not dilated. They and the alveoli in all the consolidated areas are filled with blood-corpuscles in which there are found a few small mononuclear cells and an even smaller number of larger mononuclears. Polymorphonuclear leucocytes are very scarce. The whole consolidated part of the section is so densely filled with extremely well preserved red corpuscles that it is very difficult to make out the nature of the other changes. Neighboring alveoli contain fluid with very few cells of any kind. There is but little fibrin visible in the alveoli, which are distended with blood, and no capillary thrombi are seen. The epithelial cells are partly desquamated, but many swollen cells of this order are found adhering to the walls. Some, and, indeed, the majority of the alveoli, show no bacteria whatever, but in others there are numerous large round Gram-positive cocci, sometimes in short chains, oftener in groups and occasionally in large solid masses composed of many thousands. These are evidently the staphylococcus aureus found in culture. In other areas and especially in the bronchioles, a few pneumococci are visible. No especial destruction of tissue or intense reaction is found about the large clumps of staphylococci.

Closer examination of the cells of the alveolar exudate shows that many of them are about as large as red corpuscles, or slightly larger, with sharp outline and a small, solid, round, densely stained nucleus. These are similar to those described elsewhere. There are also definite lymphocytes which are quite distinct, and fairly numerous larger mononuclear cells with a vesicular nucleus and basophilic protoplasm. All the cells are very well preserved.

Case 5714.—H. G. F. Age 30. Onset on the morning of October 1, 1918, with slight coryza and general aching in the lumbar region and legs.

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These symptoms increased until October 3, with headache, sore throat, burning of the eyes, photophobia and cough, with expectoration of thin tenacious, purulent sputum. Temperature 100-103°. The patient was drowsy, cold and prostrated. Leucocytes 4760-6400. The lungs were negative except for some impairment of the right back below the scapula, with numerous râles. Pharynx much injected. Cyanosis marked. The extremities were cool in spite of high fever. Died October 7. Autopsy 11 hours after death.

Anatomical Diagnosis.—Confluent lobular pneumonia.

The *left pleura* contains a small amount of dark brown fluid. The surfaces are smooth and glistening.

The *right pleura* shows the same appearance as the left.

The *left lung* is heavy and rather firm. It is dark purplish red with numerous irregular areas of firmer consistency, exceptionally closely placed in the lower lobe posteriorly and separated by wider areas of air-containing tissue in the upper lobe. These patches are not very firm and not very sharply outlined but are airless and project slightly. The intervening tissue is filled with a reddish fluid which exudes readily upon the surface. The bronchi are deeply reddened and this reddening extends into the trachea and larynx.

The *right lung* presents the same picture as the left.

Cultures from the lungs, pleural fluid and trachea contain Pneumococcus Atypical II and also Strept. hæmolyticus, which was cultivated also from the blood.

Microscopical Examination.—The lung presents the most beautiful type of fresh consolidation following influenza and usually found to be caused by the pneumococcus. In this case organisms are few in the bronchioles and still fewer in the ductuli and tissues of the lung, but there are several kinds, not only pneumococci but staphylococci, probably streptococci and large stout bacilli. No influenza bacilli are to be found. Some of the lung substance shows simply an extreme œdema with dilatation of the capillaries. The remainder is distinguished by the very great dilatation of the ductuli alveolares which become very conspicuous. They contain fluid which is in part coagulated in fixation but very few cells of any kind. There is no fibrin coagulum and only a few leucocytes and red corpuscles. Here and in the larger bronchioles, whose epithelium is partly desquamated but whose walls are not thickened or infiltrated, most of the bacteria are found. The surrounding alveoli contain a loose network of fibrin often pressed back against the wall and relatively few leucocytes. The latter are in a perfect state of preservation and so are the few red corpuscles mingled with them. There are always several of the small rounded cells with a deeply stained solid-looking single round nucleus and what seem to be neutrophile granulations. Other larger mononuclear cells with a vesicular nucleus and faintly granular protoplasm are also present. It seems possible that these larger cells may be myelocytes, and that in spite of the usual idea of the metamorphosis of myelocytes into polymorphonuclear leucocytes, the small granular cells may

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represent some form intermediate between myelocytes and leucocytes. The epithelium is not very well preserved and much of it is desquamated.

The ductuli are usually thickly lined with homogeneous hyaline material so often described, and in places this extends into, and occupies part of the cavities of the adjacent alveoli. The capillaries which immediately underlie the hyaline material are commonly obliterated by fibrin, so that no blood passes through. This is true elsewhere, too, as can be well seen in Weigert preparations, but it is most striking just where the hyaline forms.

The pleura is œdematous but not otherwise greatly altered; the interlobular septa are also œdematous and slightly infiltrated. Lymphatics are not conspicuous. The bronchi are, as already mentioned, not especially thickened or infiltrated and the same applies to the blood-vessels.

In this case, although there was a great mixture of organisms, it seems probable that the pneumococcus played the principal rôle.

CASE 5722.—S. G. Age 10 years. Onset October 7, 1918, with slight fever, a little cough and epistaxis. He seemed to improve until October 14 when he complained of pain in the head and stomach. Admitted to the hospital on October 16 with cough, rapid respiration, fever, prostration and stupor. Respiration shallow and labored. Impairment of resonance in left axilla and left back with suppression of breath sounds and tubular quality. Numerous râles everywhere. Leucocytes 3840. Temperature 102.4°. Died October 16. Autopsy 17 hours later.

Anatomical Diagnosis.—Lobular pneumonia with fibrinopurulent tracheitis; mediastinal lymphadenitis.

Left Pleura.—The left pleural cavity contains about 50 c. c. of slightly turbid yellow fluid. The posterior and interlobular surfaces are dull, and show a deposit of gray fibrin.

Right Pleura.—The right pleural cavity also contains a small amount of turbid fluid. The pleura is roughened laterally and posteriorly with thin deposits of fibrin.

Left Lung.—The upper lobe is smooth and air-containing anteriorly, but posteriorly it is solid and dark, slaty purple in color with smaller areas of air-containing lung. The lower lobe shows extensive consolidation posteriorly. The inferior surface is mottled by consolidated and air-containing lobules. The cut surface of the upper lobe is red and firm and somewhat roughened. That of the lower lobe shows in its upper half a solid gray area which stands above the surrounding surface and oozes a purulent material with a small abscess here and there, while in its lower half it is like the upper lobe, blood-stained and œdematous. The bronchi are deeply reddened and contain a frothy yellow fluid.

Right Lung.—The right lung is rather larger than the left. The anterior portion shows paler pinkish-gray areas alternating with deep reddish-brown patches which are solid. The posterior portions of the lower lobe are solid and slaty purple in color, although the anterior parts are mottled as above. On section the upper lobe shows solid areas of deep red. In

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the lower lobe the consolidated area is more grayish and stands above the surrounding surface, being composed of small gray foci with red periphery.

Larynx.—The mucosa of the larynx and glottis is deeply reddened and covered with a grayish exudate which extends downward into the trachea.

No cultures were made.

Microscopical Examination.—The sections show a peculiar combination of many features which may perhaps be explained by the fact that while the predominant and wide-spread organism is a pneumococcus, many areas of the lung swarm with the influenza bacillus or at least with a bacillus morphologically identical with it.

The pleura is covered by a very thin film of fibrin. The tissue is spread apart by œdema and in the lymphatics there is much fluid, a few leucocytes and pneumococci. The interlobular septa are inconspicuous. The bronchial walls are widened by œdema and by an infiltration of mononuclear cells. Their lymphatics are not greatly dilated. The epithelium is loosened but in the larger branches continuous. The contents are purulent, with pneumococci and influenza bacilli. The smaller branches have lost their epithelium and their walls are covered with a dense layer of fibrin infiltrated with leucocytes and mononuclear cells. The walls of these small bronchioles are greatly thickened by an infiltration of mononuclear wandering cells. But most striking is the great accumulation of masses of influenza bacilli in the diphtheritic pseudomembrane which forms the lining. Pneumococci are there, too, but not in such huge numbers.

The ductuli alveolares are, in places only, dilated and thickly lined with hyaline material. They contain no dense exudate but great numbers of mononuclear cells with leucocytes. The alveolar walls are not thrombosed, although they are often stretched so that the capillaries appear bloodless. In patches, sometimes of large extent, they are packed with an exudate composed chiefly of leucocytes with much disintegrated granular swollen cell bodies. Pneumococci of typical form are scattered in the exudate in great numbers but very few influenza bacilli are seen. Outside such dense areas of consolidation there is much of the lung which is merely œdematous or very sparsely infiltrated with leucocytes. In this œdema fluid there are scattered many pneumococci and also clouds of influenza bacilli. Toward the pleura the alveoli are large and are packed with disintegrating leucocytes. It is only in the marginal alveoli where a loose exudate persists that many red corpuscles are found.

It is to be observed that the alveolar epithelium, in general thin and stretched or desquamated, becomes high and cubical in certain groups of alveoli where the interstitial infiltration and rigidity of the walls are most marked.

Case 5726.—A. M. Age 13 months. Onset October 12, 1918, with fever and cough. Admitted to the hospital October 17 in a state of prostration and stupor. Respiration labored, chiefly thoracic; dullness in left axilla

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and over right back. Dry râles heard everywhere. Leucocytes 3640. Died October 18. Autopsy one hour after death.

Anatomical Diagnosis.—Lobular pneumonia; fibrinous pleurisy; fibrinopurulent tracheitis; bronchitis.

The *left pleura* contains 20 c. c. of yellow turbid fluid.

The *right pleura* contains 75 c. c. of turbid yellow fluid. The surfaces are smooth but there is a little loosely adherent fibrin.

Left Lung.—The left lung shows small patches of consolidation in the anterior portions and a much larger area involving almost the entire posterior portion of the upper and lower lobes. Where these dark red consolidated areas reach the surface there is a dull exudate of fibrin on the pleura. On section the more extensive posterior portions are grayish red, dull, roughened and elevated. The scattered patches anteriorly are deep red, not so firm, and only slightly elevated.

Right Lung.—The same description applies to the right lung.

The *trachea* and *larynx* show marked hyperæmia.

Cultures.—Gram-positive diplococci but all were overgrown by a spreading Gram-negative bacillus.

Microscopical Examination.—The pleura is covered by shreds of fibrin but its substance is loaded with bacteria. So, too, the interlobular septa are greatly widened and in places contain bacteria. The lymphatics are distended with leucocytes and bacteria both there and in the walls of the bronchi and vessels. The bronchi retain fairly well their epithelium. The ductuli alveolares are greatly dilated and beginning in the bronchioles *over* the epithelium there is the layer of hyaline material so often described, running down into the ductuli and continuing even into the alveoli. This overlies but does not necessarily replace even the alveolar epithelium. The lung is consolidated only in patches and is not especially œdematous elsewhere. These patches are almost necrotic and most of the alveolar walls show stagnant capillary blood columns or actually thrombosed capillaries. The ductuli appear as pale spaces with little but fibrin, the alveoli contain leucocytes with many large and small mononuclears. The whole area is densely loaded with bacteria sprinkled and crowded everywhere. These are usually single, rather pointed at the extremities, stout but with distinct polar staining, the central part remaining unstained by the gram stain. No other bacteria are seen. They do not look like pneumococci although pneumococci alone are reported in culture.

Case 211.—J. L. J. Onset September 17, 1918, with headache, backache, fever, cough and prostration.

Admitted to hospital September 19. Next day pain in left lower chest. Physical signs of consolidation in left base posteriorly and lower right scapular region on September 21. Patient became delirious and died September 26. Sputum not examined. Autopsy September 27, 1918, 18 hours after death.

Anatomical Diagnosis.—Confluent lobular pneumonia, acute tracheitis and laryngitis. Infection of antrum. Acute splenic tumor.

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The *left pleural cavity* contains no excess of fluid; surfaces smooth with some flecks of hæmorrhage. *Right pleural cavity* contains no fluid and the surfaces are smooth but slightly dulled over the projecting solid patches in the lung where they are blood-stained and of a brick-red color.

Left Lung.—Both upper and lower lobes are air-containing anteriorly but there are areas of consolidation in the lower and posterior portions of each lobe. The area of consolidation in the upper lobe is about 6 cm. in diameter and is not perfectly uniform, being rather patchy. On section the bronchi are reddened and their walls dull looking, but otherwise not altered. They contain a frothy brownish blood-stained fluid. The blood-vessels and interlobular septa are unchanged. The alveoli are evidently filled with exudate throughout, patches of greyish pink color which are surrounded and separated by dark red areas. In the lower lobe there is a similar group of patches of greyish pink firm tissue interspersed with dark red areas. Isolated patches with greyish centers have a hæmorrhagic margin and the large group is bordered by hæmorrhage. The mucosa of the bronchi is very hyperæmic.

The *right lung* (Fig. 8) is extremely voluminous and the whole posterior part of the upper lobe is consolidated. The middle lobe has only a few nodules of consolidation, whereas the lower lobe presents several widely separated firm areas, the whole posterior and lower part as well as a large area in the upper and anterior part being affected. On incision there is found in the upper lobe a sharply outlined irregular patch of consolidation which is greyish red with scattered patches and a general border of hæmorrhage. In the lower lobe there are numerous ramifying patches of elevated consolidated tissue which has a uniform greyish red color except for a few hæmorrhagic patches, and is surrounded by a deep red margin. The consolidation appears to be due to an intra-alveolar exudate. The bronchi are not especially altered and contain no yellow exudate. The intervening and surrounding lung substance is normal; the blood vessels, interlobular septa and lymphatics seem normal.

The *spleen* and mesenteric lymph glands are somewhat swollen.

The *vocal cords* (Fig. 9) are covered with an opaque chaff-like substance and appear slightly ulcerated. The mucosa of the trachea is deeply reddened and covered with a ragged greyish yellow exudate in a fine network. The antrum contains a purulent exudate.

Cultures from the lungs and from the antrum showed the staphylococcus albus and the influenza bacillus. Those from the heart's blood contained the staphylococcus alone.

Microscopical Examination.—The trachea is intensely hyperæmic and its walls in many places are infiltrated with extravasated blood. The mucosa is partly covered with a rather dense fibrinous exudate which is continuous with the underlying necrotic tissue. Where this pseudomembrane has fallen off there remains a shallow ulceration. In these areas staphylococci and influenza bacilli are found.

The lung shows very sharply outlined patches of consolidation in which the pleura and interlobular septa are not especially altered. The bronchi

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have as a rule lost their epithelium. The larger ones show a distinct diphtheritic or pseudomembranous inflammation with which there are associated staphylococci in great numbers. Influenza bacilli are doubtfully made out. The walls are rather thickly infiltrated with leucocytes and mononuclear cells.

The fresh cut surface of the consolidated area has a coarsely spongy appearance which is explained by these sections. Viewed with a lens the sections have also a spongy appearance and the coarser openings are found to be the ductuli alveolares which contain no cellular exudate but are spread wide with fluid and lined with a rather thick layer of hyaline material which does not take the Weigert fibrin stain or at least only in part. The intervening air-cells are packed with an exudate of polymorphonuclear leucocytes, mononuclear cells and relatively little fibrin. To the unaided eye these alveoli look opaque and form the separating walls between the much wider ductuli alveolares. They contain staphylococci among the cells of the exudate. In the margins of the areas there is no real zone of hæmorrhage but rather one of hyperæmia. Nevertheless, there is much œdema throughout the solid part and many of the alveoli within the consolidation contain an exudate composed almost wholly of blood. All the cells of the exudate are very well preserved and even the red blood corpuscles maintain their outlines perfectly. The hyaline material is not limited to the ductules but extends in some cases into the alveoli in a thin layer. The consolidation is fairly uniform throughout the affected patches and even where the staphylococci occur in clumps in the air-cells there is nothing resembling an abscess.

Case 6143.—L. W. Age 38 years. Onset February 5, 1920, with acute illness of febrile character. The patient was brought to the hospital February 8 in a comatose condition. Temperature 100-101° with evidence of consolidation in the left lower lobe and beginning consolidation in the right lower lobe. Died February 9. Autopsy nine hours after death.

Anatomical Diagnosis.—Confluent lobular pneumonia; serofibrinous pleurisy; rupture and hæmatoma of the rectus abdominis muscles.

Rectus Muscles.—The rectus muscles from the level of the umbilicus to the pubes are greatly distended with masses of extravasated blood coming from a large tear in the middle of the muscle.

The *left pleura* contains 300 c. c. of slightly turbid, straw-colored fluid. There are a few old pleural adhesions. The pleura is in general smooth.

The *right pleura* contains also 300 c. c. of slightly turbid, straw-colored fluid. In its posterior portions over the surface of the lungs there is a thin fibrinous exudate, but otherwise the surface is smooth.

Left Lung.—The upper lobe anteriorly is pale and air-containing. The posterior and inferior aspects of the upper and lower lobes are bluish-red in color and present numerous nodular, solid masses. On section the anterior part of the upper lobe is air-containing but all the rest of the lung is dark red, spongy in texture, elastic, but without giving any crepitation. In the posterior part of the lower lobe there are numerous large, dry, red, granular elevated areas which become confluent.

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A few similar areas are found in the posterior part of the upper lobe. They are inelastic, in contrast with the surrounding moist elastic lung substance. The interlobular septa are not prominent. The bronchi contain dark brown mucus. The bronchial nodes are soft and not enlarged.

Right Lung.—The upper lobe and the anterior part of the middle lobe are air-containing; the surface smooth and glistening. The lower lobe and the posterior part of the middle lobe are dark red, firm and elastic and contain no air. On section the cut surface is dark red, moist and elastic with an occasional small, elevated, red, granular area.

The larynx and trachea are very slightly reddened.

Cultures from the lung show the staphylococcus aureus in pure culture. No other organisms were found in the smear.

Microscopical Examination.—The surface of the lung shows no fibrinous exudate. Indeed, the lining cells of the pleura are beautifully preserved. The pleural membrane and the interlobular septa are widened and show numerous wandering cells of which the majority are rather large mononuclears with bluish-staining protoplasm and a round vesicular nucleus with coarse, deeply stained clumps of chromatin. There are also a few polymorphonuclears in this framework. The bronchi are denuded of their epithelium in the larger branches; in the smaller the epithelium in sheets lies free but there is nothing else except fluid in these bronchioles. The tissue of the wall of the bronchi thus exposed is not necrotic and there is relatively slight infiltration of the bronchial walls.

The ductuli alveolares are extremely wide and contain coagulated fluid with very few cells. There is a very distinct lining layer of hyaline material which caps especially the projecting points in the wall and extends even into the alveoli. Wherever it appears it overlies the epithelium, if any remains. The alveoli are also in many places greatly dilated, although in others where they are most filled with exudate they are normal in size. Their epithelium is in many places desquamated in part, in part swollen but retained upon the wall. The consolidation is a very irregular one, none of the ductuli containing any cellular exudate, while the surrounding or intervening alveoli are loosely or more densely filled. Some alveoli in great groups are very loosely occupied, and at its densest the exudate is rather open and quite fresh and well preserved. Some groups of alveoli contain a large proportion of red corpuscles but in most these are less conspicuous. A delicate network of fibrin stretches through them and there are rather numerous polymorphonuclear neutrophiles. There are also many of the small sharply outlined cells with a solid, deeply stained, round nucleus. These have neutrophilic granules exactly like those of the polymorphonuclears and seem to be in some way related to them. The great number of rather large mononuclear leucocytes in the alveolar exudate is striking. These are basophilic cells with a large, round, vesicular nucleus with chromatin in dense large masses but no very conspicuous nucleolus and are thus easily distinguished from the epithelial cells, which, when desquamated, still show the characteristic nucleolus. Painstaking search through the section of the lung from which it was

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known that the staphylococcus aureus was cultivated revealed only four or five Gram-positive cocci of the appearance of staphylococci. While it is thus evident that staphylococci were there, they were certainly present in very small numbers, hardly enough, it would seem, to account for the pulmonary lesion.

In phagocytic cells and lying free in the alveoli there are many minute irregular bodies apparently with a chromatin fleck or even a rather distinct nucleus. These lead one to reflect upon our dependence upon the regularity of form of everything that can be recognized as a parasite. There could be no better disguise for the undiscovered ætiological agent of influenza than some such irregularity of form which would allow it to be permanently disregarded and considered to be nuclear debris.

Case 5706.—Mrs. G. S. Aged 35 years. Onset on September 28, 1918, with a shaking chill and loss of appetite; no pain; slight cough. Severe cough on September 29 with scanty sputum. Admitted to hospital September 30. Temp. 103°; pulse 120; resp. 28. Dyspnœa; cyanosis; no definite dullness over the lungs but many moist râles. Leucocytes 11,700. At 11.30 p. m. orthopnœa; rapid respiration with extreme cyanosis; coma. Still no areas of consolidation present. Died at 3.20 a. m. October 1. Autopsy three hours later.

Anatomical Diagnosis.—Clinical history of influenza. Confluent lobular pneumonia, bilateral; chronic mitral and tricuspid endocarditis with stenosis; chronic passive congestion of the lungs.

The *left pleura* contains 150 c. c. of cloudy yellowish fluid with a few small particles of fibrin. The posterior surface of the lungs shows several small patches roughened by a thin layer of fibrin. Elsewhere the surfaces are glistening.

Right pleura contains 100 c. c. of similar fluid. Surfaces glistening except for a few small patches posteriorly where the gloss is lost.

Heart.—There is some thickening and insufficiency of the tricuspid valves and extreme stenosis of the mitral valve.

The *left lung* is voluminous; the bronchus contains a thin, frothy fluid, and its mucosa is very much congested. The upper lobe is rather firm and elastic and on section is extremely moist, dark red, very spongy and presents patches of a slightly firmer consistency which are somewhat elevated but not very different in color. The lower lobe presents little air-containing tissue. On section it shows a somewhat more extensive consolidation that that of the upper lobe. The cut surface is a dark red color, very moist, and covered by a thin, turbid fluid. The lymph glands at the hilum are large and deeply pigmented with numerous small caseous foci.

The *right lung* is also heavy, large, and rather elastic. The upper lobe on section shows some small areas which are slightly prominent but not markedly distinguished from the surrounding tissue by their color. The cut surface is very moist and dark red and markedly spongy. The anterior portion and the whole mid-lobe show no consolidation but are very œdematous. The lower lobe on section oozes a great deal of frothy

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fluid. The prevailing color of the cut surface is dark red. There can be palpated numerous rather small areas of firmer texture which extend through the whole lobe and involve more than half of its substance. These firmer areas are also moist and dark red in color.

The mucosa of the pharynx is deeply congested. The tonsils are of moderate size.

Cultures from the blood were negative. Those from the lung showed a hæmolytic streptococcus and a doubtful short Gram-negative bacillus.

Microscopical Examination.—There is marked inequality in the development of the lesions in different areas, for while certain patches show a definite pneumonia most of the sections reveal only an œdematous condition with the exudation of very few leucocytes and red corpuscles.

The pleura is not altered except that there is œdema in places. The interlobular septa and all the other structures belonging to the framework of the lung are unchanged. The bronchi show some desquamation of the epithelium but contain only coagulated fluid with a few cells. The ductuli alveolares are greatly widened and lined with a thick hyaline layer which extends far into the alveoli. This is far more conspicuous in the lung in general than in the patches of pneumonia. The alveoli are distended with fluid with little or no fibrin. Their epithelium is not especially altered, although many alveoli contain masses of pigmented heart-failure cells and there are other evidences of chronic passive congestion. No bacteria were found in such areas.

The more definitely consolidated areas present an exudate which is very fresh and well preserved and composed of a delicate network of fibrin with numerous red corpuscles and a few polymorphonuclear leucocytes. There are also many small mononuclear cells with densely staining solid-looking small round nucleus and faintly granular eosin-staining protoplasm. These are such cells as have been described before in early stages of pneumonia. There is no infiltration of the walls of bronchi or alveoli.

Practically no bacteria are to be found even in these areas. Most careful search over several sections showed only about 10 Gram-positive cocci in pairs or short chains. These look like pneumococci, although nothing was found in culture except a hemolytic streptococcus.

The short course of the illness and the freshness of the tissue make it seem that this material is especially valuable in approaching the unimpeded study of the effects of epidemic influenza itself. It is interesting that in the areas in which there is no definite pneumonic exudate, the hyaline lining of the ductuli is already well developed as though it were the product of the influenza process itself and independent of bacteria. The extreme rarity of bacteria will probably account for the very fresh character of the pneumonia, if indeed the pneumonia is necessarily to be ascribed to bacteria.

Case 83.—G. P. Was ill for three days in his tent with headache, pain in the neck, weakness, cough, frequent urination, and aching in the

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legs and body. Admitted to hospital October 4, 1918, with increased vocal fremitus in the back and front of chest and harsh breath sounds. On October 9 there was some dullness with râles over both backs and bronchial breathing at the right base. On October 10 there was flatness over the right base behind and areas of dullness over the left back at the base. Delirium on October 11. Temperature range 101-103.° Pulse 90-120. Resp. 20-48. Died October 12. Autopsy three hours later.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia.

Rectus muscles normal.

The *left pleura* contains about 80 c. c. of opalescent fluid. The surfaces are moist and glistening.

The *right pleura* contains no excess of fluid. The surfaces are in general smooth but there are patches of opaque brick red discoloration.

Left Lung.—Most of the upper lobe is air-containing, but there are lobular areas of consolidation (Fig. 10). Practically the whole lower lobe is firm. On section the upper lobe shows consolidated areas which are greyish red, coarse and spongy as though composed of thick-walled air cells filled with fluid. The interlobular septa and bronchioles in each lobule are conspicuous. The whole lower and posterior part of the lower lobe is firm, elastic, extremely moist and mottled with greyish red and dark red areas. The cut surface is spongy and oozes fluid but no definite plugs of exudate are seen. Sections through the anterior portion show the same condition.

Right Lung.—The upper lobe presents two large masses of consolidation, one in the anterior upper portion, the other at the lower margin, posteriorly. The posterior part of the mid-lobe is consolidated and practically the whole of the lower lobe. The bronchial glands are large, moist and soft. These areas of consolidation present on section the same appearances as seen in the left lung. The bronchi and bronchioles are especially conspicuous and contain a little muco-purulent material.

The larynx and trachea are only slightly hyperæmic.

The bone-marrow is fatty with a few red areas.

The sphenoid, ethmoid and frontal sinuses were examined and the two latter contained a somewhat blood-stained exudate.

The brain and meninges are normal.

Cultures and even the study of smears from the lungs were unsatisfactory. A Gram-negative coccus was found in smears, but nothing grew in culture. Injected into a mouse the material from the lung caused a streptococcal infection in the heart and peritoneum which is not to be relied upon. Cultures from the trachea gave the bacillus of Pfeiffer and a pneumococcus. Those from the ethmoid and frontal sinuses gave the Pfeiffer bacillus and staphylococci or streptococci.

It appears that the only trustworthy evidence as to the pulmonary infections in this case must come from smears and sections of the lung and in these a large Gram-negative diplococcus is found in numbers and alone. It seems possible, therefore, that the organism concerned may have been a meningococcus although the meninges were normal.

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Microscopical Examination.—The pleura shows little alteration from normal except areas of hæmorrhage. The interlobular septa are œdematous and rather wide. The lymphatics are greatly distended with a practically clear fluid. The bronchioles contain a purulent exudate. Their epithelium is intact, their walls slightly œdematous and infiltrated by a few wandering cells which are chiefly rather large mononuclears without definite granules in the protoplasm. There are a few mast cells with distinct basophilic granulations. Beyond this there is no alteration of the framework of the lung and the alveolar walls are practically unchanged. The ductuli alveolares are, however, greatly dilated with fluid containing a few leucocytes and their walls are covered, especially over projecting points, with the hyaline layer so often described. The alveoli contain in the more densely consolidated portions an exudate very largely made up of red corpuscles. It is closely packed and there is little fibrin or fluid. Near by, however, in the less densely consolidated part there is much fluid in the alveoli and polymorphonuclear leucocytes are practically the only cells present. In the densely packed alveoli there are relatively few of these leucocytes—in their place are great numbers of small cells such as were described in Case 82, cells about 9μ in diameter which are quite round and sharply outlined, red-staining, slightly larger than red corpuscles and with Wilson's stain coloring a rose pink with fine granulations in contrast with the rather orange red corpuscles. They contain a small round nucleus which stains a dense blue black and shows no sign of vesicular structure. With iron hæmatoxylin and Mallory's connective-tissue stain these cells show a gray blue protoplasm in sharp contrast with the orange of the red corpuscles, but they are quite unlike lymphocytes. The leucocytic exudate in the minute bronchioles is loaded with Gram-negative cocci, chiefly intracellular and often arranged in pairs or in groups of four. These are hardly to be found in the alveoli. No other bacteria are found.

Case 226.—S. O. Admitted in coma on September 30, 1918, and died October 1, 1918, without having regained consciousness. Temp. 103-104°. Resp. 28-30. Pulse 136. No further history.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia with old pleural adhesions (right). Excessive coal pigmentation of lungs.

Rectus muscles apparently normal.

The *left pleura* contains about 300 c. c. of brownish, fairly clear fluid. The surfaces are glistening but flecked with deep purple patches and brown stains.

The *right pleura* shows a few old adhesions over the apex of the lung. It contains only about 20 c. c. of fluid and the remaining surfaces are smooth and glistening but marbled with blackish or deep purple discolorations.

The *left lung* is very voluminous and heavy. There are patches of air-containing lung on the upper anterior part of the upper lobe and the extreme anterior border of the lower lobe. All the rest is consolidated. The upper lobe shows deep indentations produced by old scars and there are corresponding adhesions.

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On section there is an extensive black pigmentation which makes it difficult to distinguish pneumonic areas but it appears that there are many consolidated areas scattered among air-containing tracts and patches of induration caused by the anthracosis. These areas of consolidation are spongy and coarse as though formed in an emphysematous lung and show no distinct plugs. The same condition is found all through the lung even in the most anterior parts. It is noteworthy that there are many lobules sharply outlined by the interlobular septa in which there is no pigment whatever.

The *right lung* shows precisely the same conditions as described for the left. The upper lobe is almost entirely filled with lobules consolidated partly by pigmentation and partly by the pneumonic process. The bone-marrow is brown and gelatinous but fairly firm.

Cultures show in both lungs a hæmolytic streptococcus together with the staphylococcus albus; in the pleura, heart's blood and pericardium a pneumococcus. The spleen is negative but lungs and pleura show also a Gram-negative bacillus. Smears from the lung show only round Gram-negative cocci.

Microscopical Examination.—The sections of the lung show in all parts about the same changes. It is difficult, on account of the great amount of coal pigment with its corresponding scarring and induration of the lung, to observe clearly the more recent pneumonic changes, but there are unpigmented areas where the conditions appear clearly in certain areas. The pleura is pigmented in a patchy way and the interlobular septa which are spread wide by accumulations of fluid show bands of pigment along their edges in the adjacent lung tissue. The fluid in the œdematous septum itself contains none and the broad lymphatic channels are quite free from it. The consolidated lung is closely intermingled with the scarred pigmented area, but all the lung substance even in the non-pigmented lobules is extremely œdematous and contains little air. The bronchioles and ductules are extraordinarily dilated and filled with fluid. The ductules have a typical thick lining of hyaline material especially laid down over the more prominent points. The epithelium is only partly desquamated. The alveoli round about these are filled with a very fresh exudate in which mononuclear cells are very prominent and polymorphonuclear leucocytes rather few. The red corpuscles are well preserved. Of the mononuclear cells there are, as before, large irregular cells with a pale vesicular nucleus which seem to be desquamated epithelial cells, large and small deeply staining mononuclears with basophilic protoplasm which appear to be polyblastic wandering cells, and then small cells about the size of red corpuscles with small solid deeply stained green and greenish black nucleus and red finely granular protoplasm. These, of course, should be comparable to lymphocytes, but when they are contrasted with obvious lymphocytes which lie nearby in the bronchial wall it is seen to be impossible to include them with these. I have had the suspicion that they must be normoblasts since their staining characters are exactly those of nucleated red corpuscles, but it is somewhat difficult to accept their presence

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in an inflammatory exudate in the lung. The capillaries are little if at all thrombosed.

In the exudate no great numbers of bacteria are to be found except in some of the alveoli where there are many cells loaded with cocci. These are large rounded Gram-negative cocci usually in pairs but often closely clumped together in fours or larger packets. They are nearly all intracellular, enclosed in leucocytes or mononuclear cells. No Gram-positive cocci were found.

From this it would appear that the predominant organism which also appears as such in the smears from the lungs was missed in the cultures which yielded staphylococci and streptococci and even pneumococci.

The case loses its value to a great degree on this account, but it is interesting to speculate upon its nature. It suggests itself that this may be a meningococcus which failed to appear in culture media not especially planned for it or where other less abundant bacteria overgrew it. The fact that the man was comatose when admitted and until his death suggests the possibility that he may have had also a meningitis, but the head was not opened. In any case the lung shows the most beautiful example of the hyaline deposit in the ductuli and it is interesting that the type of bacteria concerned does not seem to govern the appearance of that material.

The separation of this group of cases from that which follows is quite arbitrary and depends only upon the presence of that peculiar dilatation of the ductuli alveolares, with a hyaline lining deposit which has impressed every observer in the examination of the lungs of many of the persons dying in the epidemic of influenza. Although this lesion is associated with the freshest and best preserved inflammatory exudate in the lungs and usually with a relatively moderate bacterial infection and is rarely found in such lungs as present a densely packed exudate of partly disintegrated cells with enormous numbers of bacteria, it cannot be said that the average duration of the disease is shorter in this group than in the next. In both death occurred after an average duration of ten days. It is an unfamiliar lesion although it has been found also in the lungs of persons dying after exposure to war gases and in those of some animals after the experimental insufflation of certain chemicals.

If we group the cases together merely on the basis of the presence of this lesion, it is found that the group is far from homogeneous as far as the bacteria are concerned and in many instances there are very few bacteria indeed, so that it requires long search in the affected tissue to find one. Pneumococci are preponderant in most of the cases and are sometimes present in rather large numbers. Sometimes they

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are in pure culture, sometimes mixed with other bacteria. The staphylococcus aureus was the only bacterium in one case, mixed with a few influenza bacilli in another. In the freshest case of all (5706), in which death occurred three days after the first symptom, the lesion under discussion was very well developed although only an occasional streptococcus could be found after long search. Two other cases showed the presence of a Gram-negative coccus which may have been the meningococcus.

The suggestion readily arises, therefore, that this lesion may be independent of the secondary bacterial invaders and due to the epidemic disease influenza itself. Tempting as this hypothesis is, it is far from being proven, although the early stages of experimental pneumonia produced by the intratracheal insufflation of pneumococci and influenza bacilli show nothing of such a lesion (Blake and Cecil).

The lesion itself is very striking. The bronchioles are relatively unchanged but where they lose their cylindrical epithelium and pass over into the ductuli alveolares there begins a marked dilatation sufficient to produce cavities easily visible to the naked eye on the cut surface of the lung and very conspicuous in sections. The alveoli themselves are scarcely dilated but are filled with a fresh exudate of fluid with a network of fibrin and blood corpuscles and leucocytes which are relatively few but in a perfect state of preservation. The dilated ductule is filled with fluid with very few red corpuscles and scarcely any leucocytes so that it appears in the fresh lung as containing a rather gelatinous pink clear fluid. The projecting septa which mark off the atria, and indeed all the walls of the ductule, are covered with a thick layer of homogeneous hyaline pink-staining material which does not give the reaction for fibrin. Usually the lining epithelial cells have disappeared but occasionally they are present in remnants buried underneath the hyaline layer. In most cases it is evident that the hyaline layer is formed over the surface of the epithelial cells and in one (5726) it may be traced for a long distance over relatively unaltered epithelium.

In few cases is this alteration of the ductules universal and in general it is a change which is to be found only in the less advanced areas of consolidation and is not recognizable in the patches of dense exudate. In Case 224 the change in the whole lung is so homogeneous that this feature is found everywhere. In Case 5706 it is most evident in areas where there is only œdema and engorgement but practically

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disappears in the patches of denser consolidation. So, too, in Case 223, there are certain zones in which the whole picture is most beautifully shown while in the other parts of the lung, where all the spaces are packed with leucocytes, the ductuli still seem rather wide but show only the faintest line of hyaline material which cannot be distinguished easily from the abundant fibrin now filling the lumen and buried among leucocytes.

When we turn to the cases of the next group, the existence of such alterations in the ductuli could never be suspected. It is difficult even to outline the ductuli and there is no sign of hyaline lining—everything is packed with a dense cellular exudate.

From this it might be argued, on the one hand, that the lesion is produced by the invading bacteria or, on the other, that it is a specific product of the epidemic disease influenza. If we suppose that the bacteria produce it, we must believe it to be the effect of a mild infection, since it appears only in those cases in which there are rather few bacteria, or in the outlying zones of the area of consolidation, and we must suppose that an intenser bacterial infection prevents its appearance or later obliterates it. Against this theory stands the fact that this lesion is not observed in the pneumonias that occur at times when there is no epidemic of influenza and does not appear even in the early stages of those experimental pneumonias produced in animals by the insufflation of the bacteria found in these cases into the trachea (Blake and Cecil).

If we suppose that the epidemic disease influenza produces the lesion, we must recognize the fact that it is not found in all the cases, even though all of the patients have had influenza. Indeed, some of the cases in which the gross appearance of the lungs at autopsy is marked by the characteristic hæmorrhagic œdema fail to show this lesion of the ductuli, although the exudate in the alveoli is quite fresh. Those lungs in which bacteria are present in overwhelming numbers, accompanied by a dense exudate of leucocytes which is closely packed and much disintegrated, fail to show this lesion and those in which the hæmolytic streptococcus is the organism which in great numbers dominates the scene, show no trace of it.

Therefore, apparently we may surmise that the rapid development of great numbers of bacteria tends to prevent the appearance of the lesion or, if it is already present, to destroy it by removing the hyaline material and allowing the ductuli to contract again to their normal

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size. On this theory the bacteria, when too few, fail to disturb it and it persists, no matter what the character of these sparsely scattered organisms.

The question cannot be answered positively with our present information, but it must be evident that we lean to the theory suggested by Goodpasture, that this is a lesion specifically related to the influenza itself and not to the secondary bacterial invasion. That it is a process associated with considerable injury to the underlying tissue is shown not only by the usual destruction of the epithelial cells but at times by the thrombosis of the capillaries which lie directly beneath it.

In all these cases emphasis has been laid upon the extreme freshness of most of the exudate which presents iteslf in the lung at autopsy as an intensely hæmorrhagic fluid easily escaping in large quantity from the cut surface and generally accompanied by a delicate network of fibrin not sufficient to confer on the lung tissue anything more than a moderate increase in its elastic consistency. In the cases in which this form of exudate is present alone and in which there are no areas of denser consolidation, it is rather difficult to be sure that there is really any consolidation, although the associated pleural and other hæmorrhages, the congestion of the bronchial mucosa and the distention of the lymphatics in the pleura and interlobular septa, make it fairly obvious.

In the exudate itself the extremely good state of preservation of the freshly emigrated cells make it possible to stain sharply whatever granules are present with the aid of such stains as Wright's or Wilson's. The large proportion of mononuclear wandering cells in the intra-alveolar exudate is especially striking and, indeed, in some cases the distinctly recognizable polymorphonuclear leucocytes seem to be rather in the minority. Many of the mononuclear cells are somewhat larger than lymphocytes with a relatively large vesicular nucleus with deeply stained chromatin clumps and bluish cytoplasm. These we have interpreted as belonging to the group of lymphocytes with their later modification. They are often to be found in the substance of the tissue especially about the bronchioles and small vessels where they occasionally come to resemble plasma cells. Cells with distinctly basophilic granules in the cytoplasm are rare. They are sometimes found, especially in the meshes of the tissue, but probably not more frequently than in a normal lung. Epithelial cells from the alveolar walls undoubtedly drop off into the exudate and become rounded. It

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seems possible to recognize these by their very distinct nucleolus and it appears that they do not form any very great proportion of the cells present.

Most abundant, however, is another cell which has been mentioned with varying hypotheses, in the description of each case. This is a small cell only slightly larger than a red corpuscle, quite round and sharply outlined with a single small round nucleus which stains solidly black or bluish black or green, and with its cytoplasm filled with neutrophile granules. Such cells are always present in the exudate of the cases of short duration and sometimes outnumber the polymorphonuclear leucocytes. They have not been observed to act as phagocytes, but, although we have entertained many theories about them, it seems most probable that they belong to the developmental stages of the polymorphonuclear. They seem to correspond with the "pseudolymphocyte" described by Ehrlich as a degenerative form of the leucocyte or an incompletely developed transition from the myelocyte. Naegeli mentions these as occurring in severe infections and sometimes in the blood of children. These are vague statements and it is difficult to conceive of these cells as representing degenerations of completely formed polymorphonuclear leucocytes. It seems more plausible to regard them as abortive attempts at the formation of polymorphonuclears from myelocytes and to explain their appearance, in such numbers and in such perfect and characteristic form, as representing the type of cell produced in an emergency which called for great numbers of neutrophile leucocytes. This is a matter, however, which requires further study and little more can be done here than to point out their extraordinary abundance especially in the early stages of the pneumonia and to emphasize the fact that they are by no means irregular structures such as might be expected if they represented the products of degeneration of some other cell.

The exudate in some of the cases, as for example in 223, has brought about a peculiar condition in the alveolar walls which seems to make very plain the fact that a delicate structureless membrane upon which the epithelial cells lie may be lifted away on each side from the central meshwork of capillaries. Leucocytes and fluid accumulate between the capillaries and this membrane, and cause an enormous swelling of the wall. In this instance the epithelial cells have been desquamated and the membrane is partly covered by the hyaline layer.

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Several of the cases in this and in the following groups present also a peculiar appearance in the pleural membrane which we have not encountered except in this epidemic. The surface of the lung may be smooth and glistening over most of its extent but discolored in places by large irregular patches of a dull red stain resembling red paint. This is found to be caused by the extravasation of blood in the crevices of the superficial layers of the pleural membrane. In the same cases there are often found, as in 222, 223, 82, etc., small discrete or confluent rounded patches which are smooth, convex, slightly elevated and of a pale grayish brown color, like coffee with cream. These on section prove to be almost solid accumulations of pneumococci in the substance of the pleural membrane. They are associated with a more diffuse distribution of these bacteria in the pleura at large and also in the interlobular septa.

GROUP 2.—*Cases terminating fatally with great numbers of pneumococci in the lung and elsewhere, and with a diffuse pneumonic consolidation in which the peculiar changes in the ductuli are masked or absent.*

The following group of cases is also far from being homogeneous in the details of the gross and histological changes in the lungs or even in the character of the bacteria present, but the cases may properly be brought together, inasmuch as the predominant organism in each was the pneumococcus and inasmuch as the general character of the pulmonary change was uniform. In these the duration of the illness which led to death was practically the same as that in the preceding group, but bacteria are present in the tissue in far greater quantities and in accord with this it is found that the bronchioles and alveoli are packed with a dense cellular exudate. They differ from the preceding group only in the intensity of the bacterial infection and the corresponding reaction except in that they do not present the dilatation of the ductuli with hyaline lining upon which that group was collected.

CASE 216.—F. E. M. Onset September 12, 1918, with frontal headache, cough, anorexia, fainting, chills and pain in the abdomen. No epistaxis, nausea or vomiting. The patient entered the hospital September 24 in a subconscious condition. Temp. 103°, pulse 104, resp. 26. Drowsiness and dyspnœa. Conjunctivæ jaundiced, mouth foul, lips cyanotic. Throat slightly inflamed. Dullness from the 5th interspace to the lower axilla with hyperresonance between the 2d and 5th rib on the left side. On the right there is dullness over the back, with bronchial breathing and râles.

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Blood Count.—	Leucocytes	Differential count Polym.	S. M.	L. M.	Tr.
September 23	8000	59	32	5	4
September 25	8800	79	10	4	7
September 26	10400				
September 27	8350				

Died September 27 at 7.30 p. m. Autopsy September 28 at 4.50 p. m.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia. Bilateral fibrinopurulent pleurisy with old adhesions. Hyperplasia of bone-marrow.

The *left pleural cavity* contains 200 c. c. of thick turbid fluid. The surfaces are covered with a loose, rather slimy exudate of fibrin which is thick between the lobes and on the mesial and diaphragmatic surfaces but readily slips off, showing numerous hæmorrhages on the reddened surface.

The *right pleural cavity* is partially obliterated by old adhesions. In the upper portion there is a free area which contains a little thick turbid brownish fluid and is lined with a thin fibrinous exudate.

Left Lung.—The upper lobe is air-containing except for the part which adjoins the interlobular cleft where there is a uniform area of consolidation of a dark greyish red color, each alveolus containing an opaque plug of exudate. The lower lobe appears to be almost entirely consolidated and presents a quite different appearance. It is mainly occupied by a large area of complete consolidation which is pretty sharply outlined although it is surrounded by a somewhat less definitely consolidated portion. This area is almost white, although there is a large dark red patch in the centre. It resembles more a carcinomatous mass than a pneumonic consolidation. The lowermost part of the lung is less firmly consolidated and is dark greyish purple with much evidence of collapse. There is, however, embedded in it and bulging from the diaphragmatic surface a round nodule of the same light-colored firm consolidation. The bronchi are dark red and exude a thick opaque fluid.

The *right lung* is blue and heavy. The whole posterior portion of the upper lobe is consolidated (practically none of the middle lobe), and the whole lower portion of the lower lobe (Fig. 11). A large mass projects from the diaphragmatic surface which is firm and very pale. On section the uppermost part of the upper lobe is found to be air-containing, the lower part forming a mass, about 7 cm. in diameter, which is firm and in general dark greyish red with some central white patches. The lower lobe shows some of these dense greyish red areas of consolidation surrounded by a zone of collapse, but the greater portion of it is occupied by a densely consolidated area, the outer part of which is nearly white, while the central part is deep purple and slightly sunken below the level of the rest of the consolidated tissue. The bronchi are deeply reddened and sometimes contain moulds or casts of fibrin. The larynx is not inflamed; the vocal cords are intact.

Cultures from the autopsy showed Pneumococcus Type IV in the lungs, pleura and heart's blood. Those from the spleen and pericardium were

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negative. A staphylococcus was also found in the right pleura. No influenza bacilli were found.

Microscopical Examination.—The pleural surfaces of the left lung are devoid of covering cells, but the fibrinous exudate has disappeared. The pleura itself is infiltrated with blood and in places with leucocytes. The interlobular septa are not prominently thickened and contain relatively few wandering cells. Nor are the bronchial walls or blood-vessels markedly infiltrated. Occasional blood-vessels can be found in which the endothelium is lifted up by accumulations of leucocytes and in places the outer walls and those of the bronchi contain a few mononuclear wandering cells. The bronchi show almost everywhere an extensive, if not complete, desquamation of the epithelium. The walls are not thickened. The lumen contains a mass of purulent exudate with little blood. Some bronchi are plugged with dense fibrinous masses which extend a long way and form a mould of the lumen.

The areas of consolidation are uniform in character except that the marginal portions are deeply hæmorrhagic, while the more central portions are densely packed with leucocytes without admixture of blood. A typical condition is found in sections which pass through the marginal part of one of the large white areas. The deeper alveoli are widely distended by being filled with the densest possible exudate of leucocytes, most of which are fragmented, with fine granular dust of nuclear material, although a great many are still well preserved. There is a network of fibrin which in some places is fairly dense, in others delicate and fibrillar. The alveolar walls are stretched out thin, devoid of epithelium and almost entirely empty of blood. They do not appear to be necrotic and no hyaline thrombi are found. The cells contain pneumococci and a great many of these organisms are scattered free. Most of them still stain well and there is no such extreme phagocytosis as is visible in some other cases and even in the smaller foci of consolidation in this case. No other organisms are to be found in these densest areas of consolidation. As one passes into the margin of the area the exudate becomes less densely packed and the alveolar walls less stretched. The exudate looks fresher and the cells better preserved. Bacteria disappear almost completely, but enormous numbers of red corpuscles are present, often agglutinated into small masses in the alveoli. There is no evidence of rupture or necrosis of the alveolar capillaries which are distended with blood. The contents of the bronchi show numerous pneumococci, many of which are enclosed in leucocytes and have lost their positive Gram-staining. There are also rather numerous minute organisms in these leucocytes which are Gram-negative and occasionally rod-shaped. They are rather too plump to be influenza bacilli. Since no influenza bacilli were recognized in culture or smear, I incline to the idea that these are partially digested remains of pneumococci. Practically none of them are free and they differ in appearance from the influenza bacillus in their form and in their arrangement. None of these have been found in the alveolar exudate.

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In addition to the pneumococci and these doubtful organisms resembling influenza bacilli, there are in the bronchi, and in the alveoli in certain limited areas of the consolidated tissue, great numbers of large gram-positive bacilli. These are as large as the gas bacillus of Welch, stain irregularly and have slightly rounded ends. Their nature is unknown.

The histological conditions in the right lung are practically identical with those in the left.

The other organs show no definite abnormalities.

Case 217.—F. M. Onset on September 6, 1918, with headache, fever and chills. On September 10 cough with blood-stained sputum. Entered the hospital September 18, and on September 22 there was flatness and bronchial breathing over the left lower lobe with increased vocal fremitus, cyanosis and dyspnœa, throat dryness and congestion of the throat, resonance impaired on both sides behind. On September 27 emphysema developed over the neck and supraclavicular fossæ, and before death the crackling had extended down over the chest. Died September 29 at 4 a. m.

Blood Count.—		Differential count			
	Leucocytes	Polym.	S. M.	L. M.	Tr.
September 23	4500	76	14	10	
September 25	3500	79	8	13	
September 26	2700	60	31	9	
September 27	4500	80	15	5	

Autopsy six hours after death.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia. Hæmorrhagic pseudomembranous laryngitis. Subcutaneous and generalized emphysema.

There are no external abrasions or wounds. The neck is greatly swollen and this swelling extends up on the cheeks, especially on the left side and down over the front of the chest where the subcutaneous tissue crackles on pressure. The skin of the whole flank on the left side is ballooned up with gas and there is a similar but less extensive emphysema of the right side. The legs and external genitalia are not emphysematous. The abdominal organs show no abnormalities, but the diaphragm is emphysematous.

Left Pleural Cavity.—All the mediastinal tissues are puffed up with bubbles of gas and hang like froth from the outer surface of the pericardium in the pleural cavity. The cavity contains 100 c. c. of brownish fluid. The surfaces are smooth but stained with a characteristic brick-red stain over the firm lower lobe. There is emphysema of the interlobar and interlobular tissue.

The *right pleural cavity* contains no excess of fluid; the surfaces are smooth and glistening, but there is marked emphysema of the interlobar tissue and of the interlobular septa.

The *heart* in general is normal; the myocardium is not emphysematous and the blood not markedly laked.

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Left Lung.—The upper lobe is air-containing in the upper and anterior portions, but there are some firm areas in the lower posterior part. The lower lobe is really air-containing only in the lower anterior marginal portion. The rest is heavy, flabby and fairly firm, but not rigid or hard. Insufflation sends a little air into the superficial part of this consolidated area.

On section the solid patch in the upper lobe is fairly uniform, dark greyish red, much elevated and with prominent alveolar plugs of exudate. The lower lobe shows a very rough cut surface because it is studded with groups of projecting yellow plugs of exudate which are usually surrounded by hæmorrhages. In this respect the consolidation resembles that in Case 215, since there are many small discrete patches which represent the consolidation of a few alveoli, each patch being separately surrounded by hæmorrhage.

The *right lung* is voluminous and heavy. The anterior part of the upper lobe seems to be air-containing although one can feel nodules throughout it. The posterior part is depressed, blue and solid. The mid-lobe is air-containing throughout. The lower lobe in its anterior part is air-containing. The posterior part is firm.

On section the upper lobe shows in its lower mesial portion a fairly uniform greyish red consolidation. This area is spongy and the terminal bronchioles stand open as spaces filled with fluid but without distinct plugs of exudate. The consolidation has reached different stages in neighboring lobules and in some of those which are sharply outlined the exudate seems paler and denser, but even these are still spongy. The lower lobe contains a large irregular central and posterior conglomeration of groups of lobules which are consolidated. They are dark greyish red and stand up above the surrounding air-containing lung. They contain no air, but there are no distinct projecting plugs of exudate. Instead, each terminal bronchiole or ductulus alveolaris is filled with a reddish fluid. The areas are therefore distinctly spongy and not rigid, although elastic and fairly firm. The interlobular septa are normal. The bronchi are not especially reddened, but contain a frothy fluid which is not noticeably purulent in character.

Organs of the Neck.—The uvula and epiglottis are swollen, reddened and covered with an opaque bran-like material. The whole lining of the larynx is similarly swollen and reddened and the vocal cords touch the false cords obliterating the space between. They are all covered with the same opaque bran-like material which also adheres to the mucosa of the trachea below. Still further down the trachea is reddened and there are points of hæmorrhage and little adherent flecks of opaque yellow material.

Cultures were not taken at the autopsy.

Microscopical Examination.—Sections through various areas of consolidation in the lungs show essentially the same type of alteration. The pleura is not thickened and only slightly infiltrated in patches with blood. The interlobular septa are narrow and inconspicuous. The bronchi are filled with a closely packed exudate of leucocytes with some fibrin. Their epithelial cells are in part desquamated and the walls show a few wander-

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ing leucocytes. In the case of some of the very small bronchioles the epithelium is all lost and the wall is densely penetrated by elongated nuclei of leucocytes which appear to have been caught in the act of wandering. The endothelium of the blood vessels is sometimes lifted up by leucocytes, but in general there is no especial infiltration of the framework of the lung. Nevertheless in places the septa and even the lung substance itself are torn apart by accumulations of gas or air. No reaction and no necrosis is visible in the edges of these bubbles and no gas bacilli can be found there. The exudate in the lung substance is not entirely homogeneous, but in places occurs in patches with the central bronchiole full of exudate surrounded by a group of alveoli filled with leucocytes in the more central region and with blood at the periphery. In the larger areas there are patches in which the alveoli are especially densely packed with leucocytes. On section these appear as the more blue-stained, solid areas separated by spongy and hæmorrhagic tissue. When viewed with a lens it is seen that the ductuli alveolares stand wide open, giving the whole area a spongy appearance. They contain only coagulated fluid. When closely examined the alveolar walls are found to be stretched and anæmic, but nowhere necrotic. The exudate in the more central alveoli is composed of leucocytes and desquamated epithelium. These are very much disintegrated and ragged. In the peripheral alveoli in each of the confluent patches the leucocytes are fewer and better preserved and there is an abundance of red corpuscles. There are occasional groups of alveoli in the walls of which leucocytes are very numerous, stretched out into bizarre forms as though wandering.

The alveolar and bronchial exudate contains practically no bacteria except pneumococci. These are very clearly recognizable by their form and staining. In the more central and densely consolidated alveoli the pneumococci show advanced disintegrative changes; polar staining, swelling, fragmentation and reduction to dust-like particles leave hardly any of them well preserved. No influenza bacilli can be found anywhere. In some of the larger bronchioles there are very many large Gram-positive bacilli with rather square ends. These are of about the size and shape of gas bacilli, but since they do not occur especially in relation to the interstitial bubbles of gas it is difficult to interpret them as such. In contrast to the findings in Case 213, which were distinctly due to infection with Welch's gas bacillus, the tissue in this case is nowhere necrotic, there is no laking of the blood and such gas as escaped at the autopsy would not ignite.

It seems probable, therefore, that this case of interstitial emphysema was due to the mechanical introduction of air into the tissue, as has been so often observed.

Case 225.—E. A. Began on September 24, 1918, to feel ill with headache, cough, backache and general aching of the bones. Admitted to hospital September 26. On September 29 slight dullness and crepitant râles over right lung in front and back. Respiration labored. Not delirious. Temp.

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101-102°. Pulse 120-140. Resp. 48-60. Died October 1, 1918. Autopsy two hours after death.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia. Old pleural adhesions (left); hyperplasia of bone-marrow; horseshoe kidney.

Rectus muscles, normal.

The *left pleural cavity* is partly obliterated by old adhesions, the interstices of which are filled with about 50 c. c. of clear fluid.

The *right pleural cavity* contains about 5 c. c. of rather turbid brown fluid. The surfaces are smooth and glistening, but deep blue in the posterior part and discolored with patches of dark red opaque blood-stain.

The *left lung* is everywhere roughened by old adhesions which are coarse and especially thick between the diaphragmatic surface and the diaphragm, where they are distended with fluid and form a gelatinous mass.

The upper lobe is air-containing in its upper and anterior portion, but the lower posterior part is firm, studded with hæmorrhages and rendered irregular by projecting masses over which there is a dull paint-like dark red stain. The lower lobe, except for the lowermost margin, seems completely consolidated; is also flecked with hæmorrhages and presents prominent nodules.

On section the upper lobe shows several patches of uniform consolidation about 3 cm. in diameter, occasionally reaching the surface. These are spongy, moist, greyish red, with wide ductuli containing only fluid except in a few small patches where opaque plugs project.

The lower lobe, which is completely consolidated, is mottled with dark red and lighter greyish red patches. All of these exude quantities of fluid and especially in the darker patches show a coarse spongy structure full of fluid. The lighter patches show a few opaque projecting plugs. The connective-tissue framework is normal.

The bronchial glands are enlarged, grey and moist.

Right Lung.—The upper lobe is consolidated behind, showing several large masses; anteriorly and at the apex it is air-containing. The middle lobe shows two large, firm masses posteriorly; the anterior part is air-containing. The lower lobe is entirely consolidated posteriorly, its anterior portion air-containing.

On section the upper lobe contains large, irregular, red spongy, moist patches which are firm, elastic, pit on pressure and exude a quantity of fluid and blood, but show no opaque plugs. They are especially dark in color in this lung. The middle lobe contains a similar dark red, spongy, moist area. The lower lobe shows in its posterior portion the same dark red œdematous tissue which in places is almost black. It is very boggy and full of fluid, but presents no visible opaque plugs.

The *bone-marrow* is chocolate brown with some flecks of fat. It is fairly solid and comes out of the shaft of the femur in the form of a cylinder.

The *larynx* shows no ulceration, but the trachea is slightly injected.

Cultures from the right and left lung, right pleura, heart and pericardium show Pneumococcus IV in pure culture. Smears from the lung show pneumococci alone, and sections give the same result.

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Microscopical Examination.—Sections of the lung show some portions quite free from exudate. Sharply marked off from these by widened œdematous interlobular septa are consolidated areas or lobules in which the alveoli are tightly packed with exudate. Some groups of alveoli are so filled that no space remains between the cells and all are necrotic. The pleura is hyperæmic and œdematous and is covered with a fibrinopurulent exudate in which there are great numbers of pneumococci. The interlobular septa are widely distended and contain dilated blood-vessels, large lymphatics full of leucocytes and other cells. The tissue is infiltrated with leucocytes, mast cells and mononuclear wandering cells of various sizes. Pneumococci occur in groups. The bronchi contain leucocytes and a little fibrin; the epithelium is sometimes lifted up by accumulations of leucocytes. The walls are not much infiltrated with cells.

The alveolar walls are not thickened or infiltrated. Their epithelium is peculiarly distinct and with Giemsa's or Wilson's stain the purplish finely reticulated protoplasm of the cells is seen to be rather abundant and to be able to give off processes to the underlying tissue in cases where the sheet of epithelium has been lifted up by leucocytes. The epithelial cells are sometimes in mitosis, they are rarely phagocytic while still attached to the wall. Many of them are desquamated and so long as they can be distinctly recognized are not phagocytic. There are, however, many large mononuclear cells of rather similar appearance, in the alveoli, which are phagocytic and engulf other cells.

The alveoli contain many red corpuscles, a predominant number of polymorphonuclear leucocytes and many mononuclear cells. Of these mast cells form a small proportion, lymphocytes are present but in small numbers; larger wandering mononuclear cells with a vesicular nucleus and rather basophile protoplasm are quite numerous. It is, however, the neutrophile leucocytes which seem to increase in numbers as time passes. There is a relatively slight network of fibrin in most of the alveoli and pneumococci are found only with difficulty. There is no hyaline lining of the ductules.

Case 227.—W. F. Admitted September 29, 1918, with consolidation of the lower right lobe. Cyanosis, signs of pulmonary œdema. Temp. 104-97°. Pulse 94-120. Resp. 15-36. Died October 1, 1918. Autopsy one hour later.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia.

Rectus muscles seem normal.

The *left pleura* contains no excess of fluid. The surfaces are glued together slightly by fresh fibrin and roughened by it. There are a few old adhesions over the apex and posterior part of the lung.

The *right pleura* contains about 100 c. c. of turbid fluid and shows fairly fresh adhesions between the mesial surface and the pericardium, as well as over the diaphragm. These enclose a considerable quantity of fluid so that when they are liberated the cavity contains about 250 c. c. of fluid in all. The surfaces are studded with hæmorrhages.

The *left lung* is rather firm in the posterior lower part of the upper lobe and in the posterior part of the lower lobe, but these areas are relatively

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soft and elastic. There are firmer masses, however, in the lower or diaphragmatic surface of the lower lobe.

On section the upper lobe appears to be practically entirely air-containing. In the lower lobe there is a very large central and posterior area of consolidation and other nodules more anteriorly placed. The consolidated portions are œdematous, spongy and dark greyish red, but in the centre of the largest one there are six or seven lobules which are much denser and more prominent. Some of these are opaque red, others opaque yellow, and from them project rough plugs of exudate. The bronchi exude a brown frothy fluid; their walls are pale.

The *right lung* is very large and heavy (Fig. 12). Only the upper and anterior part of the upper lobe is still air-containing. On section much turbid chocolate-colored fluid runs from the cut surface. The upper lobe is dense, reddish brown in its lower part, œdematous and boggy, pitting on pressure, coarse, spongy and containing no definite plugs of exudate but only fluid.

The lower lobe shows the same condition in its upper part, but in the lower portion there is an area about 6 cm. in diameter which is firmer than the rest and stands out prominently. It is composed of many lobules whose outlines are visible and from the cut surface of which project many plugs of exudate. This part is pale greyish red with flecks of opaque yellow. It merges into the firm œdematous surrounding tissue which slopes away from it and is smooth, shining and deep red. The bronchi contain a thick turbid brownish fluid and occasionally fibrinous moulds.

The *bone-marrow* is gelatinous and yellow, flecked with red but fairly firm.

The *larynx* and *trachea* are normal.

Cultures from the left lung, right lung and right pleura, heart's blood, spleen and pericardium show Pneumococcus IV in pure culture, although in the right pleura and heart's blood there were contaminating organisms. The smears from the lungs show the pneumococcus alone. Sections from trachea and lungs show the same organism alone.

Microscopical Examination.—The sections are chiefly from the more densely consolidated portion of the right lower lobe and present a rather thick, fibrinous exudate upon the pleural surface. The pleura itself is swollen by an accumulation of fluid containing immense numbers of pneumococci. Most of the cells are reduced to nuclear fragments and the lining cells are lost. Over this is the layer of rather dense fibrin which is everywhere perforated with vacuoles which are full of micrococci. The interlobular septa are very widely spread apart by fluid and cells with enormous numbers of bacteria. The lymphatics, where seen, are not definitely thrombosed. The bronchi and bronchioles are filled with a purulent exudate rich in bacteria. Their epithelial lining is usually preserved intact, but their walls are much infiltrated with wandering cells. So, too, the walls of the blood vessels are infiltrated with cells which often lift up the endothelium.

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There is no dilatation of the ductuli alveolares nor any hyaline deposit. They, like the alveoli, are widely distended by a cellular exudate with a delicate network of fibrin. This exudate is everywhere strewn with great numbers of bacteria. The alveolar walls are distinctly distended, and, while they show blood-containing capillaries in most cases, in many of them the capillaries contain no blood and appear to be obstructed. The epithelial lining cells are in most places remarkably well preserved.

The exudate is in many areas very densely packed. It is everywhere mixed with red corpuscles, but some groups of alveoli contain a far higher proportion of red cells than others, so that such patches look red. The greatest variety of cells is present, but the character of the exudate is practically the same everywhere. Polymorphonuclear leucocytes are most numerous and are actively phagocytic, often being literally stuffed with pneumococci. In addition there are many cells of a kind described in other cases, the exact nature of which it is hard to decide since they do not correspond precisely with any well recognized type. These are smaller than the polymorphonuclear leucocytes, rather sharply outlined and round. They have a single round very deeply stained solid nucleus and a cytoplasm which takes a dense eosin stain or is faintly granular with the Romanowsky stains, taking about the same tint as the neutrophile granules. The sharp circular outline of these cells and the fact that they are not definitely found to be phagocytic even when they lie in the midst of great numbers of bacteria and leucocytes packed with bacteria should give some suggestion as to their nature. They are easily distinguished from lymphocytes which are present elsewhere in the same preparations by every character. Morphologically they resemble normoblasts in many respects, but the cell outline is not so sharp as in those elements, and I cannot convince myself that they could be present in such numbers without having been observed in the circulating blood. There are also many large mononuclear wandering cells of highly phagocytic character which take up leucocytes and cell fragments. These are evidently derived from the group found infiltrating the bronchial and blood-vessel walls. In those situations every type of mononuclear freely wandering cell is found, from the typical lymphocyte through all gradations to the very large cell with vesicular deeply staining nucleus and abundant cytoplasm with indefinite scattered granulations and bluish staining cytoplasm. Some of these contain many rather fine granules which stain blue black in the Giemsa preparations and are easily distinguished from the occasional mast cell with its conspicuous violet basophile granules. Eosinophiles are not seen, but megalocaryocytes are easily visible in many of the capillaries of the alveolar walls in this as in all the other cases.

Pneumococci are present in enormous numbers and evidently in pure culture as prolonged search through the section fails to show any other organism.

Case 229.—J. F. N. Onset on September 21, 1918, after exposure to wet and cold in a tent, with chills, headache, backache and fever. The patient

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was admitted to the hospital on September 26 with pain in head and back. Bronchial breathing and râles in the right lower lobe. Delirium, coma. Temp. 102-107°. Pulse 84-144. Resp. 2-64. Death October 1, 1918.

Autopsy twenty-five minutes after death.

Anatomical Diagnosis.—Confluent lobular pneumonia; chronic endocarditis with mitral stenosis.

Rectus muscles normal.

The *left pleura* contains no fluid; surfaces smooth and glistening.

The *right pleura* contains 100 c. c. of fluid. The surfaces, especially over the back of the lung and the diaphragmatic surface, are roughened with fibrin; the same is true of the mesial surface.

The *left lung* is voluminous and in large part air-containing, although there are in both upper and lower lobes darker purplish patches which are slightly firmer than the rest. On section there is very little definite consolidation in the upper lobe. In the lower there are dark-colored patches which are spongy and œdematous but not firmly consolidated.

Right Lung.—The upper lobe is air-containing anteriorly, flabby and dark in color posteriorly. The middle lobe is air-containing throughout. The lower lobe is consolidated throughout, firm and rigid, with whitish masses showing through the pleural surface. The bronchial glands are enlarged, dark grey and moist. On section the upper lobe is air-containing except in its lower part where there is an elastic, spongy and œdematous area. The lower lobe shows on section a fairly rigid general consolidation of which the more mesial portion seems older and, although smooth and in general greyish white, shows distinct yellowish plugs of exudate. The remainder is dark greyish red, mottled with paler areas and is smoother and moister than the rest. The bronchi are pale.

The larynx and trachea are normal.

Cultures from the right and left lung, from the heart and from the pericardium show Pneumococcus Type IV, but the lungs and pericardium show in addition Gram-negative bacilli, some of small size and hæmoglobinophilic, others very coarse. From the heart's blood there was cultivated also a Gram-negative diplococcus. Culture from the spleen was negative.

Microscopical Examination.—The pleura over sections of the left lung is smooth. The lung substance is extensively filled with coagulable fluid, the ductuli alveolares remaining empty and giving the spongy aspect to the cut surface. There is no consolidation and the bronchi are collapsed.

Sections through the lower lobe of the right lung show a pleura covered by a thin layer of fibrin with partial destruction of the lining cells. The pleural membrane is hyperæmic, and it as well as the fibrinous exudate is thickly strewn with pneumococci in a good state of preservation. The interlobular septa are widened by œdema, a network of fibrin and an accumulation of a few leucocytes; here too the pneumococci are well preserved. The bronchi contain a purulent exudate, their walls are not especially infiltrated, but show occasional hæmorrhages, the epithelium is usually intact. The walls of the blood-vessels are slightly infiltrated and the adventitial lymphatics sometimes contain thrombi. The endothelial

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cells in some of the vessels are lifted up by accumulations of fluid beneath them. The alveolar walls are not thickened or infiltrated with cells. Thromboses of the capillaries are quite frequent and bear the relation already described to the fibrin network in the alveoli.

The alveolar exudate is dense and composed chiefly of polymorphonuclear leucocytes, although there is some admixture of red corpuscles with a few of the small mononuclear cells with small dense, pycnotic nucleus described in other cases. There are also a few large mononuclear wandering cells with slightly basophilic protoplasm and deeply stained vesicular nucleus. The leucocytes contain very numerous bacteria, and wherever these can be actually recognized they have the morphology of pneumococci. Most of them, however, are fragmented, or almost completely disintegrated, and stain very irregularly. In this respect the bacteria in the alveolar exudate contrast very sharply with those lodged in the substance of the pleura or in the interlobular septa where they are very well preserved. The alveolar epithelium is in most places almost intact, although lost in many alveoli. The alveolar capillaries as usual frequently contain megalocaryocytes.

It appears that in this case the exudate has already encompassed the destruction of most of the bacteria with which it has come into immediate contact.

In the opposite lung large bacilli are often found in the œdema fluid in the alveoli, but no bacilli or gram-negative organisms can be seen in the consolidated areas just described.

Case 85.—T. L. Aged 21 years. Onset on October 3 with cough, headache, nausea, weakness and general aching, stiffness of neck and back. Admitted to hospital October 3, 1918, with tubular breathing in the left lower lobe and rough breathing on the right side. On October 12 a pleural rub developed on the left side. Temp. 102-103°. Pulse 90-108. Resp. 24-60. Died October 13. Autopsy three hours after death.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia; infection of sphenoid sinuses.

Conjunctivæ and mucosæ jaundiced.

Rectus muscles normal.

The *left pleural* surfaces are slightly glued together by fresh fibrin and the lower half of the mesial surface shows a layer of fibrinous exudate. The upper and anterior surfaces are glistening. There is no fluid.

The *right pleura* contains no fluid, but over the posterior portion of the lung there is a thin layer of fresh fibrinous exudate which roughens the surfaces. The upper and anterior surfaces are smooth.

Left Lung.—The bronchus exudes an abundance of brownish red, frothy, mucoid fluid. The bronchial glands are slightly enlarged. The upper lobe is air-containing except for a patch of consolidation in its lower anterior portion which on section shows a greyish red, œdematous, spongy surface. The bronchi are somewhat reddened. The lower lobe is firm and rigid throughout. On section it is entirely airless, dark greyish purple and very moist. It is studded thickly with irregular confluent patches of grey, dry,

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rough, consolidated tissue in which it is evident that the alveoli are filled with plugs of exudate. This is not a uniform consolidation, but is interspersed with dark red areas, some of which are firm while others are spongy, soft and œdematous.

Right Lung.—The bronchi exude the same sort of fluid as in the left lung. The bronchial glands are much enlarged and are dark greyish red. The upper lobe is consolidated in its lower and posterior portions. It is dark red, airless and covered with a fibrinous exudate. On section the consolidated tissue is brownish red, extremely moist, rather gelatinous and spongy, but through it there runs a ramifying confluent network of denser areas which are opaque, yellow and rough. The bronchioles exude a viscid brown fluid, but are not exceptionally hyperæmic or thickened. The lower lobe is air-containing in its anterior margin and the whole posterior part is firm, dark red and covered with a fibrinous exudate which is stained in places with red. On section it is deep chocolate in color and exudes a viscid fluid from each part of the surface. The cut surface is fairly smooth and very moist with relatively few patches of the dry, opaque, yellow consolidation found in the upper lobe, but there are ramifying and confluent firm strands of a greyish red color which are less dry and prominent than those of the upper lobe. They show on a background of dark red, smooth, moist tissue which is quite airless.

Trachea.—Like the other organs, the trachea is jaundiced. Its mucosa is reddened but smooth and there is no ulceration of the larynx.

Sphenoid.—The right sphenoidal sinus contains 3 c. c. of turbid chocolate-colored fluid; the left contains about 1 c. c. of the same fluid. The mucosa is not reddened, but is rather greenish. The ethmoid cells contain a little of the same fluid.

Cultures.—Smears from the lung show predominating pneumococci with some influenza bacilli. Cultures from the trachea show a Gram-negative bacillus, probably Friedländer's bacillus and Pneumococcus IV, from the right and left bronchi and from the smaller bronchi the pneumococcus with great numbers of the influenza bacillus. From both lungs cultures show abundant pneumococci, bacillus influenzæ and a Gram-negative bacillus which appears to be Friedländer's bacillus. The cultures from the sphenoid showed pneumococci, the influenza bacillus and a staphylococcus.

Microscopical Examination.—The sections show pneumonic consolidation of varying degrees of intensity and in some places air-containing lung tissue of normal appearance. The pleura shows only a thin layer of fibrin with very little exudate of cells. The membrane is scarcely altered and the interlobular septa are only slightly œdematous with a moderate infiltration with leucocytes.

The bronchi in many instances have walls densely infiltrated with plasma cells and other mononuclear wandering cells. Their epithelium is generally intact or slightly dislodged, but they are full of a densely packed exudate of ragged, partly disintegrated leucocytes which are loaded with pneumococci. The number of pneumococci is overwhelming and search for other organisms is almost in vain. Some cells contain gram-

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negative particles which may be influenza bacilli, although they are not characteristic and might as well be interpreted as debris of pneumococci. At any rate, they are very few and it seems nowhere possible to recognize any great quantities of influenza bacilli in typical arrangement. Nor can other Gram-negative organisms such as Friedländer's bacillus be seen with certainty.

The blood vessels are in places thrombosed or plugged with masses of leucocytes containing pneumococci. Their walls are in many places infiltrated with leucocytes. This is a peculiar condition and it was doubted whether these might not be lymphatics instead of veins, but the size, position and the character of the walls make it clear that they are veins.

The lymphatics are dilated with fluid, often thrombosed and frequently packed with leucocytes and pneumococci.

The lung tissue itself is in places most densely consolidated, the alveoli containing so many bacteria and leucocytes as to render the alveolar walls inconspicuous, especially since in these areas the capillaries are empty of blood and often plugged with filaments of fibrin. It appears that the alveolar walls are partly necrotic in these areas. Hæmorrhage into the alveoli is more abundant round the margins of these areas. Elsewhere the exudate is not so dense and there are often air-containing alveoli or ductules interspersed. In many, however, there is a thick glutinous fluid which stains red with fuchsin and which contains vacuole-like spaces filled either with air or with a thin fluid. The latter seems more probable since these vacuoles are generally packed with bacteria. The viscid character of the fluid suggests the presence of Friedländer's bacillus, but none could be seen. The exudate is composed mainly of polymorphonuclear leucocytes with varying quantities of red corpuscles. There are some lymphocytes, but none of the small cells with deeply stained rounded nucleus described elsewhere.

There is no evident dilatation of the ductuli alveolares and no deposit of hyaline lining material.

Case 5724.—N. W. Aged 5 years. Onset about October 1, 1918, with swelling of the neck, sore throat and a bad cold. Entered the hospital October 10 with fever, drowsiness, cough and vomiting. Dullness over the back below the scapula on the left side with crackling râles and harsh breath sounds. Pharynx and tonsils red with a petechial rash on the buccal mucous membrane. Leucocytes 6960. On October 16 severe cough and consolidation of the entire right lung. Died October 17. Autopsy six hours after death.

Anatomical Diagnosis.—Confluent lobular pneumonia; fibrinous pleurisy.

The *left pleura* contains no fluid and the surfaces are smooth.

The *right pleura* contains 50 c. c. of yellow seropurulent fluid with a scattered fibrinous exudate over the surface of the lung.

The *left lung* shows a consolidation involving the posterior portion of both lobes and extending into the central portion towards the hilum. On section this is rather pale and firm and in contrast with the broad

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peripheral zone which is deep red and not definitely consolidated, but easily insufflated. The bronchi are dark red and exude a frothy red fluid.

The *right lung* is almost entirely consolidated, but there is a peripheral zone in which the alveoli are filled with a dark red fluid. The more central portion is firm, lighter in color, and rather dry-looking. The consolidation occupies large portions of both lobes.

The *larynx* and *trachea* are reddened. This reddening extends to the base of the tongue.

Cultures from the trachea, bronchi and lung show Staphylococcus aureus. Pneumococci were found in the lung and in the pleural exudate.

Microscopical Examination.—The lungs show patches of the densest possible consolidation alternating with air-containing and relatively unaffected areas. The pleura is thickened by œdema and especially by a great accumulation of bacteria. The lymphatics are greatly dilated and filled with bacteria floating in a fluid relatively poor in cells. The interlobular septa are widened, œdematous and infiltrated with mononuclear wandering cells of the usual types, including those with basophilic granulations. This is true also of the adventitial walls of the bronchioles and blood-vessels, but there is no infiltration of the alveolar walls.

The bronchi and bronchioles in many places have lost their epithelium and contain a loose exudate of leucocytes with many bacteria. The ductuli alveolares are not noticeably dilated. They, like the alveoli in these consolidated areas, are filled with a dense mass of leucocytes with relatively little admixture of mononuclear cells or red corpuscles. The cells of the exudate are loaded with bacteria and many more bacteria are free between them. Their outlines are indistinct and the granules fail to stain sharply. Most of these leucocytes appear to be disintegrated. The epithelium is partly desquamated, but even when this occurs the cells often adhere loosely to the walls. Fibrin is not especially abundant and the dense alveolar plugs visible in many of the alveoli appear to be produced by the massing together of disintegrated leucocytes. On the other hand, the capillaries in the most affected alveolar walls are completely obstructed by fibrinous strands which extend outward into the alveoli. Many of these capillaries are actually distended with bacteria and in general the enormous growth of bacteria in the substance of the tissues is remarkable. Megalocaryocytes are numerous in the capillaries where they are open and still conducting a stream of blood.

In the marginal portions of the consolidated areas the exudate is more hæmorrhagic and a few alveoli contain almost pure blood.

Cultures showed a staphylococcus aureus and a pneumococcus and in the sections it appears that the predominant organism present in enormous numbers is the pneumococcus, although in some bronchioles what appear to be staphylococci are to be seen. There are no signs of the focal development of staphylococci, however, and no characteristic focal lesions or abscesses.

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CASE 5725.—T. W. (brother of 5724). Aged 2 years. Onset on October 8, 1918, with cough and severe sweats. No fever. Chest clear. Father and mother both sick with influenza at the time. Admitted to the hospital on October 10 with a temperature of 104°, and rapid labored respiration. Leucocytes 14,640. The lungs are clear on percussion, but there are many râles over the back on the left side. On October 13 there was a friction rub with dullness in the axilla on the left side. Consolidation of the lung increased and the child died on October 17. Autopsy five hours after death.

Anatomical Diagnosis.—Confluent lobular pneumonia with fibrinous pleuritis.

The *left pleura* contains no fluid. The lung is covered with a fibrinous exudate.

The *right pleura* shows no accumulation of fluid, but the lobes are bound together by fibrinous exudate.

The *left lung* weighs 200 grams and is extensively consolidated throughout both lobes, the consolidation reaching to the posterior surface, where the pleura is covered with fibrin. In many places the line of demarcation between the consolidated areas and the relatively unaffected portion is sharp and well defined. The bronchi are intensely congested and contain a small amount of red, frothy fluid. The lymph glands are large, grey and mottled. The consolidation is uniformly greyish brown.

The *right lung* weighs 190 grams and shows quite a large area of consolidation in its more central portion involving all the lobes. Here, too, the affected lung is uniformly greyish brown. Peripherally the lung is not consolidated, but is deep red and moist.

Cultures.—Cultures show pneumococcus in both lungs. No other organisms were found.

Microscopical Examination.—The pleura over the consolidated areas is in places covered by a loose film of fibrin with many bacteria. The pleural membrane itself is spread apart by the accumulation of great numbers of bacteria, all apparently pneumococci. The interlobular septa are rather wide and the lymphatics are enormously distended in the pleura, interlobular septa and bronchial and vessel walls by masses of leucocytes with fibrin and bacteria. The bronchi are somewhat infiltrated with mononuclear cells. Their epithelium is fairly well preserved, but they contain moulds of exudate with abundant fibrin. The smaller bronchioles have in places lost their epithelium and a thick pseudomembrane of fibrin with leucocytes lines the wall and is continuous with it. The alveoli are densely filled with exudate which is composed almost entirely of polymorphonuclear leucocytes with very few mononuclear cells and little fibrin. This exudate is loaded, sometimes very heavily, with pneumococci. No other bacteria are found. The alveolar epithelium is swollen and pale and in part desquamated, but in some alveoli, especially near the bronchioles, there is a proliferation of the epithelium sufficient to fill the alveolus in part with a solid mass. The alveolar walls and bronchiolar walls in such areas are thickened slightly by infiltration with mononuclear cells of small size

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with a vesicular nucleus and basophilic protoplasm. Everywhere one may encounter a few of these deeply stained mononuclear wandering cells, usually in the walls of the alveoli.

There are some areas of especially dense consolidation in which the leucocytes of the exudate are very much disintegrated with fragmented nuclei, but there is no actual necrosis of the walls. Nor is there any capillary thrombosis in these walls. Hæmorrhage is present everywhere in slight amount, but is never very prominent. In other areas the ductuli alveolares seem to contain air, while the alveoli are filled with exudate. These are evidently near the margin of the consolidation where it passes over into the hyperæmic air-containing tissue.

Case 6133.—H. C. Aged 26 years. Onset on January 19, 1920, with chilly sensation and fever, general malaise, loss of appetite, with aching in back and limbs. On January 23 the patient stopped work on account of severe pain in the side, cough and prostration. Admitted to hospital January 29 in a semistuporous condition with respiratory distress, cyanosis, injection of conjunctivæ and pharynx; soft palate red with minute discrete white dots; dullness over both backs toward the base with widespread râles. Leucocytes 9,360. Death on January 30. Autopsy seven hours after death.

Anatomical Diagnosis.—Clinical history of influenza; bilateral confluent lobular pneumonia.

The *left pleura* contains only a few drops of opalescent fluid. The pleural surfaces are somewhat congested and there is a slight dulling of the gloss over the lower lobe of the lung.

The *right pleura* contains only a few drops of fluid. The surfaces are smooth and glistening.

The *left lung* is voluminous. The surface of the upper lobe is smooth. The lower lobe is large, heavy and solid, and flecked over its posterior and under surfaces with hæmorrhages, especially along the lymphatics. The loss of gloss is very slight and only over the posterior part. The lung substance feels very elastic and not very rigid. The bronchial lymph glands are large, soft and grayish red. The main bronchus is deep red and its lining is roughened. On section the upper lobe in its most posterior part shows patches of deep red color which are slightly firmer than the surrounding tissue. The bronchi as far as they can be traced show in their mucosa patches of green pseudomembranous exudate. The lower lobe on section shows broad consolidation which is dark greyish red in the peripheral parts mottled with deeper red and paler grey in the more central parts. One cannot make out distinctly a lobular consolidation, but the impression is received that the consolidation has proceeded from several points.

The *right lung* is more voluminous than the left. The surface in general is smooth. The upper lobe is largely air-containing, but in the lower portion posteriorly there are two firm patches. The middle lobe is air-containing except for a few small deep red patches which are firmer than

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the rest. The upper and anterior portions of the lower lobe and the most posterior part are air-containing. There is a large irregular patch in the middle of the lobe which is dark red and is overlaid by lymphatics which are distended with deep red fluid and accompanied by numerous small hæmorrhages. The bronchial glands are large and soft. The mucosa of the bronchi is deeply reddened and flecked with patches of false membrane. On section, while most of the upper lobe is air-containing, the firmer patches are seen to be solid and red in color. In the lower lobe the patches of consolidation vary greatly in size; some are very small, while others measure one or two centimetres in diameter and become confluent. The surface is slightly rough and very hæmorrhagic, but has not the extremely œdematous appearance seen in many of the cases. The ductuli alveolares are not definitely made out.

Cultures from the heart's blood show Staphylococcus aureus and Pneumococcus IV; from the lungs, Staphylococcus aureus, Micrococcus tetragenus, Pneumococcus IV; from the spleen, Staphylococcus aureus and Pneumococcus; from the trachea, Staphylococcus aureus.

Microscopical Notes.—The trachea and bronchi present the most extensive pseudomembranous inflammation with great clouds of bacteria lodged on the surface and sinking deep into the necrotic pseudomembrane and underlying tissue. These appear to be of two sorts, Gram-negative round cocci in clusters and Gram-positive organisms of the general form of pneumococci, but rather stouter. The same combination continues all through the lung.

The pleura is not covered by fibrin in the sections, nor is its tissue altered. The interlobular septa are rather broad and œdematous; they show dilated lymphatics filled with a thrombus containing pneumococci. The smaller bronchi in the lung have lost their lining, which is replaced even more completely than in the larger ones by a false membrane. The alveolar walls show no thrombosis of the capillaries, the alveoli are uniformly and densely packed with polymorphonuclear leucocytes with some admixture of red corpuscles, a little fibrin and a few mononuclear cells. Pneumococci are found scattered through the exudate, not very abundantly but rather uniformly. In certain places the whole lung tissue throughout an area of several alveoli is completely necrotic and in the midst of this there are found solid masses of the Gram-negative cocci described above. These seem rather biscuit-shaped and occur in pairs, but are densely clumped in great quantities together. A few pneumococci are found among them. They seem to produce a substance powerful enough to cause the death of the tissue, whereas the pneumococci even when closely crowded produce no such definite effect.

Case 6137.—L. C. Aged 2½ years. Onset with symptoms of influenza on January 31, 1920. The patient entered the hospital on February 2 with fever and evidences of patchy pneumonic consolidation. Leucocytes 7,800. Died February 3d. Autopsy two hours after death.

Anatomical Diagnosis.—Clinical history of influenza; acute diffuse bronchitis; lobular pneumonia.

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The *right* and *left pleural cavities* contain no fluid. The surfaces are smooth and glistening.

The *left lung* is voluminous with smooth pleura and with occasional rather large, projecting, sharply outlined areas of purplish red which are firmer than the surrounding tissue. These are especially numerous in the posterior part of the lower lobe and on section are reddish gray in color with little or no surrounding hemorrhagic area.

The *right lung* is also voluminous. The pleura is smooth and transparent, showing again occasional patches of purplish red which are sharply localized. On palpation the lung is generally air-containing, but the nodules, two or three of which appear in each lobe, are about 2 cm. in diameter, quite firm in consistency and airless. The bronchi contain a blood-tinged, frothy exudate. The mucosæ are injected and slightly roughened. On section the consolidated patches are slightly elevated and appear as greyish areas of consolidation surrounded by a hemorrhagic zone.

The trachea and larynx show no injection.

Cultures from the heart's blood show Pneumococcus II and B. influenzæ; these organisms were also found in the lungs and in the bronchial exudate.

Microscopical Examination.—The pleural surface is smooth and the directly underlying lung air-containing. There are patches of consolidation lying more deeply, but the interlobular septa and lymphatics in general are little affected. The bronchial walls are slightly œdematous and infiltrated, but very slightly so; their epithelium is fairly well preserved even into the smallest branches, and the contents are largely composed of blood and coagulated fluid with scattered groups of pneumococci. The ductuli are not especially dilated. The alveoli are filled with a fresh exudate which in the central parts of the area of consolidation is composed almost exclusively of polymorphonuclear leucocytes. These are wonderfully well preserved, and, while the neutrophilic granules show perfectly in each cell, various stages from what seems to be a myelocyte to the more advanced lobulation and deep staining of the nucleus can be seen. About the areas of dense leucocytic exudate there is a gradually fading œdema with hæmorrhage. Pneumococci are present in enormous numbers, especially in the denser exudate and especially, too, in those alveoli which border a large bronchus or vessel. In the bronchioles and in the denser exudate nothing but the pneumococcus is seen. On the other hand, in the outlying œdematous areas swarms of influenza bacilli are found in the fluid contents of the alveoli and mixed with the pneumococci. There is no chance of confusion, since the organisms lying side by side differ so greatly in size, form, and arrangement, and contrast so sharply in that the pneumococci are blue, and the influenza bacilli red in the same section.

This case resembles in the distribution of the influenza bacilli another (Case 5722), but there is no pseudomembranous bronchiolitis such as was seen there.

Case 6141.—H. H. Aged 73 years. The patient entered the hospital November 4, 1919, with carcinoma of the prostate. On January 27, 1920,

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patient began to have fever after a cystoscopic examination, and the high temperature continued for several days. Consolidation of the right base was observed on February 2. Leucocytes 6000. The patient grew worse and died February 6. Autopsy three hours after death.

Anatomical Diagnosis.—Carcinoma of the prostate with metastases; chronic diffuse nephritis; confluent lobular pneumonia involving right lower lobe with acute pleurisy.

The *left pleura* contains very little clear fluid.

The *right pleural cavity* is partly obliterated by adhesions, but contains 150 c. c. of clear fluid with floating shreds of fibrin.

The *left lung* is air-containing throughout, very pale and coarse in texture.

The *right lung* in its posterior aspect shows some dulling of the gloss of the pleural surface. The middle lobe is air-containing and densely adherent to the upper lobe. The lower lobe is very large and except for the anterior part is completely consolidated. The surface is rough and hæmorrhagic and there is a network of distended lymphatics filled with a red fluid. On section the upper and middle lobes are air-containing throughout. The lower lobe is consolidated, especially in the lower portion, where the solid portion has a spongy appearance and is of a red color. The interlobular septa are very sharply marked out and are opaque grayish white and in the lower portion of the lung very œdematous. The upper portion of the lower lobe is deep red, moist and mottled with grey patches, and exudes a quantity of turbid fluid. The bronchi are not dilated, but are reddened and contain a dark red, turbid fluid.

The larynx and trachea are normal.

Cultures from the heart's blood, right lung and trachea show Pneumococcus Type I. The trachea also contains Staphylococcus albus and Micrococcus flavus.

Microscopical Examination.—There are very large patches of rather homogeneous hæmorrhagic consolidation represented in the sections. In some of these the pleural surface is covered by a fibrinous exudate loaded with pneumococci, and beneath these areas the pleura is thickened and infiltrated and the interlobular septa, extraordinarily widened by an accumulation of exudate, extend far down into the lung. The adventitia of the bronchi is very much spread apart by this exudate, which is heavily loaded with pneumococci and the lymphatics are distended with it. The bronchi have lost most of their epithelium and contain an exudate of leucocytes. Other sections show a pleura uncovered by exudate, not infiltrated with leucocytes and with no greatly widened interlobular septa. In such parts of the lung the pneumonic exudate is rather fresher and more distinctly hæmorrhagic, but it is precisely in this part of the lung that there are found indurative changes which seem to belong to a disease of the lung antedating the pneumonia.

Everywhere the texture of the lung is very coarse—the alveoli are extremely large and irregular and their walls rather thick and dense. They are not especially infiltrated with wandering cells, nor can one discern

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any thrombi in their capillaries. The alveoli as well as the ductuli are filled rather uniformly with an exudate which is closely packed and is made up of polymorphonuclear leucocytes mixed with a little blood. The leucocytes are not very well preserved and in places seem crowded together and partly disintegrated. The same may be said of the pneumococci which are extremely numerous everywhere, but often distorted or ill-stained. No other organisms are found.

Some areas of the lung show not only thick fibrous walls surrounding the very large irregular alveoli, but dense bronchial walls and septa. The alveoli and ductuli in these areas are often lined with a thick layer of epithelium several cells deep, which in some places is almost bulky enough to fill the alveolus. It is well known that this has been described in connection with the more chronic forms of pneumonia and especially in cases of infection with the influenza bacillus. It is possible that it may be associated with the present pneumonia in this case, but the contrast between these changes and those of the actual pneumonic lesions makes this seem doubtful.

The cases detailed above present, as a rule, advanced changes in the form of a pneumonic consolidation obviously due to the pneumococci which are present throughout the exudate in colossal numbers although occasionally, as in Case 6133, the condition is complicated by the presence of a Gram-negative coccus which occurs in clumps and produces local necroses, or, as in the case of the child (6137), by the existence of influenza bacilli in the œdematous areas which surround the pneumococcal consolidation. Complicating organisms are present in some of the other cases also, but seem to exert little influence upon the lesion.

In all cases there are, in spite of the widespread areas of dense and uniform consolidation, traces of its origin as a more patchy or lobular involvement, with predominant hæmorrhage and œdema in the marginal portions, and a few have retained over considerable areas the spongy boggy consistency which was emphasized in the first group. Although the ductules are sometimes quite wide, none of these cases seems to have any remnants of the hyaline lining.

The pleura sometimes shows the red paint-like stains described above but is more often roughened by a layer of fibrin or covered by a thick honeycomb-like deposit of the same material. The pleural membrane is sometimes, but not always, thickened by an infiltration of fluid with leucocytes and mononuclear wandering cells with very numerous bacteria. So, too, the interlobular septa may in some cases be greatly infiltrated and spread apaart although occasionally they are quite

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inconspicuous. The lymphatics are moderately or but slightly distended with fluid, bacteria and leucocytes and are sometimes thrombosed.

The bronchi have usually retained their epithelium fairly well but in one case (6133), a diphtheritic exudate has replaced it far into the smallest branches. Their walls are very little infiltrated or changed in any way although the lymphatics are sometimes distended. The ductuli alveolares and the alveoli themselves are packed with partly disintegrated leucocytes among which bacteria lie in great numbers. In some cases phagocytosis of the bacteria is very striking. The distribution of hæmorrhage varies greatly but as a rule it is more intense in the marginal portions.

The bacteria are in general sharply outlined and are easily stained but in some instances, as in 229, they are in advanced stages of degeneration and disintegration where they lie in contact with the leucocytic exudate in the alveoli. In sharp contrast with this they are found to be excellently preserved in the tissue of the pleura and interlobular septa and even in the pleural exudates.

The most interesting feature of this type of pneumonia, which is in general so indefinitely characterized, is the thrombosis of some of the capillaries of the alveolar walls. Occasionally all the capillaries for some distance are obstructed but usually the occlusion affects only one or two meshes of the capillary network in an alveolar wall, all the surrounding channels being open for the passage of the streaming blood. The "thrombus" is really a closely twisted strand of filaments of fibrin which stains deeply and looks hyaline, as though a solid mould of the undulating capillary. It is rarely possible to demonstrate any special relation of the bacteria to these thrombi but there must be a local injury because leucocytes are caught stretched out through the capillary walls and the whole network of fibrin radiating into the alveoli on each side starts from this obstructed capillary (Figs. 14 and 15). The interference with the circulation in such a lung must be considerable and it recalls the injections of Kline and Winternitz which showed the great restriction of the circulation through the consolidated tissue in lobar pneumonia, although I do not remember having seen such extensive thrombosis in typical cases of lobar pneumonia.

In two of these cases, 85 and 5724, some of the capillaries have been found to contain bacteria or phagocytic cells loaded with bacteria

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and the small arterioles or venules are filled with thrombus-like masses of leucocytes.

Case 217 is one of those much discussed instances in which not only the interstitial tissues of the lung but wide areas of the mediastinal and subcutaneous tissues were blown up with air. This interstitial emphysema is evidently produced mechanically and is not due to the presence of any gas-forming organisms, but in view of the very slight cough in any of these cases it is difficult to understand it. Most of the cases which we observed clinically recovered, and in this case at autopsy we could find no satisfactory explanation of the escape of air—nor do I think that the explanations generally offered are very satisfactory. It is clear, however, that this is a phenomenon associated with the epidemic and its pneumonia and not with ordinary pneumonias.

Four cases, which on all other counts belong in this group, are separated for special consideration because, although pneumococci were cultivated from all as the predominant or even as the only organism, the cells of the exudate are filled and loaded with what appear to be Gram-negative cocci. These, since they would not grow—or at least were not grown, we cannot recognize definitely. Indeed, they are so small that I have been in doubt whether they might not be cytoplasmic granules, especially since they occur almost entirely within phagocytes or in the protoplasm of great stretching cells which lie on the alveolar walls. They stain so brightly, however, with methylene blue and similar stains, that it seems most probable that they are actual cocci. They have no resemblance in form or distribution to influenza bacilli.

What part they play in the development of the whole lesion in these lungs it is impossible to say, since in all these cases pneumococci are also present.

Other features, such as pleural hæmorrhages and bacterial flecks, capillary thrombi, even hyaline lining in dilated ductules—all are represented well in these cases and we must decide, if possible, whether the " Gram-negative cocci " have any part in their production.

Case 222.—W. O. B. Brought into the hospital September 29, 1918, unconscious, almost pulseless, cyanotic, cold and clammy. Respiration labored. Died September 29. Autopsy 14 hours after death.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia.

The *left pleural cavity* contains about 5 c. c. of fluid. The surfaces are smooth, but in places on the back of the lower lobe there are bulging flecks of a pale coffee-colored, opaque subpleural material.

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The *right pleural cavity* contains about 25 c. c. of turbid brown fluid. Its surfaces are smooth and glistening, though a little dull on the diaphragmatic aspect. They present the same elevated fawn-colored areas which seem to overlie areas of consolidation and are in or under the pleural surface.

Left Lung.—The upper and anterior parts of the upper lobe and the lower anterior margin of the lower lobe are air-containing. The lower posterior part of the upper lobe and nearly the whole of the lower lobe are consolidated, firm and elastic. On section the consolidated part of the upper lobe is brownish grey in color surrounded by a definite zone of hæmorrhage. The consolidation is more patchy posteriorly. The lower lobe is on section found to be almost completely consolidated, brownish red, smooth, elastic, rather spongy, but with distinct projecting plugs. In places the consolidation is quite sharply limited to lobules, elsewhere rather diffuse. The brownish patches in the pleura overlie the consolidated parts of the lung, but do not extend into its tissues.

The *right lung* is heavy and blue. There is a firm mass in the middle of the upper lobe and other smaller masses lie posteriorly in both upper and middle lobes. The lower lobe is entirely consolidated. On section the upper and middle lobes show areas of consolidation as indicated. The lower lobe on section is pale greyish red and minutely flecked with yellow lines. There are, however, patches of dark red. Alveolar plugs of exudate are not distinctly seen.

Organs of the Neck.—The pharynx is slightly reddened, the epiglottis, larynx and trachea also show moderate reddening. There is no ulceration, but there are some patches of opacity with surrounding congestion in the trachea just below the larynx.

Nasal Sinuses.—The sphenoid fossa contains a blood-stained fluid. The ethmoid cells are filled with a similar fluid, but the lining is not especially altered. The middle ear and mastoid cells are normal.

The *bone marrow of the femur* is composed chiefly of yellowish fat with a few brownish flecks.

Cultures from both lungs and from the right pleura gave Pneumococcus IV. Those from the lungs also showed a Gram-negative bacillus. The heart's blood and spleen showed Pneumococcus Type IV alone, while the sphenoid sinus contained both the pneumococcus and the above-mentioned Gram-negative bacillus.

Microscopical Examination.—Sections from both lungs show a very dense exudate of leucocytes and mononuclear cells, many of which are desquamated epithelial cells. In many places there is an abundant admixture of red corpuscles all fairly well preserved. The pleura is in places thickened and spread apart into several layers so that the inner limiting membrane with its elastic tissue fibres is well seen. In the patches described as visible on the surface in the form of elevated plaques of a pale brownish color, the tissue of the pleura is occupied by enormous numbers of pneumococci lying packed together and without any associated cells. The interlobular septa are not conspicuous. The bronchi contain granular

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coagulated fluid, red corpuscles, leucocytes and desquamated epithelium. Their walls are not thickened nor infiltrated. The minuter bronchioles are similarly filled with exudate, the ductuli alveolares are dilated and lined with hyaline material. Their walls and those of many of the adjacent alveoli appear to be almost necrotic, the epithelium having been desquamated. This is not, however, a very widespread condition. The capillaries in the alveolar walls are greatly dilated and the alveoli contain in addition to the cellular exudate described a great deal of fluid which has been coagulated into a granular mass.

Bacterial stains show the presence of enormous numbers of pneumococci in all the alveoli and in the bronchi. They are often in clumps and in quite long chains and are numerous in the lymphatics and in the substance of the interlobular septa and adventitia of the vessels. But there are also far greater numbers of round coccus-like bodies which are Gram-negative and stain red with the combined Goodpasture and Weigert stain or blue with the Giemsa stain. They probably constitute the abundant granules seen in the hæmatoxylin and eosin stain. All the phagocytic cells of the exudate are full of them and some are free. It might be thought at once that these were Gram-negative micrococci and their round form, about as plump as that of a staphylococcus, would support this view. But the desquamated epithelial cells are loaded with them and all the epithelial cells which line the alveolar walls in certain areas are similarly loaded. Indeed they seem to extend into depressions in the alveolar wall and to connect with similar thick layers lining the next alveolus. With the Giemsa stain they become very conspicuous as thick blue granular layers lining the alveoli. It is difficult to say with certainty what they are, although, since they are not to be found in the smear, it seems probable that they are not bacteria, but cell granules.

The tracheal mucosa is loaded with pneumococci which extend into the lymphatics.

No influenza bacilli could be found either in the lung or in the trachea.

Case 228.—R. D. C. Onset September 19, 1918, with headache, sore throat, cough and copious expectoration. Admitted to the hospital September 25, with pain in the chest and moist râles throughout the lung. Dullness and distant breathing in right back. Temp. 104-105°. Pulse 114-140. Resp. 48-56. Died October 1, 1918, at 10 a. m. Autopsy four hours later.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia; fibrinous pleuritis.

Rectus muscles normal.

The *left pleura* contains very little fluid. The surfaces are smooth anteriorly, flecked with hæmorrhage and rough with fibrin posteriorly.

The *right pleura* contains only a few cubic centimeters of fluid, but the surfaces are covered with a thin layer of fibrin which glues them together. There are numerous hæmorrhagic flecks and some large brownish red patches in the pleural membrane.

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The *left lung* is voluminous, cushiony in the upper lobe and throughout the anterior part of the lower lobe. The posterior part of the lower lobe is consolidated and rigid.

On section the upper lobe is air-containing throughout. The lower lobe in its posterior portion shows a dense consolidation filling sharply outlined lobules. Some lobules are dark red, œdematous and spongy, while all the more centrally placed lobules contain a white exudate which projects in plugs from the alveoli. The anterior part of this area of consolidation is more œdematous, but often shows numerous plugs of fibrin.

The *right lung* is very large and heavy (Fig. 13). The upper lobe is air-containing in its upper and anterior part. A firmly consolidated mass, the size of half a cocoanut, is situated in the posterior lower part. The middle lobe is air-containing except for a small part of the posterior end. The lower lobe is entirely consolidated and greatly distended. There is only a small margin of partly air-containing lung at the posterior lower border. On section the upper lobe shows the solid portion grey, rigid, mottled with dark greyish red, and with a sunken hæmorrhagic border. This patch stands out above the surrounding air-containing lung and is roughened by plugs of exudate. The lower lobe on section is covered with a glutinous exudate. The consolidated portion is almost white with patches and streaks of dark greyish red and a hæmorrhagic border which marks it off from the air-containing lung. The cut surface is very rough owing to the prominence of the white alveolar plugs. The bronchial nodes are much enlarged. The bronchi are deeply reddened and exude frothy mucus.

The larynx and trachea show no abnormality.

Cultures from right and left lung and from the pericardium showed Pneumococcus Type IV in pure culture. The right pleura contained also fine Gram-negative bacilli, but it and the heart's blood gave abundant growths of Pneumococcus IV. Cultures from the spleen were negative.

Smears from the lung show pneumococci and some Gram-positive bacillus-like forms, but no influenza bacilli. There are, however, numerous Gram-negative cocci of very small size.

Microscopical Examination.—The pleural surfaces show a thin layer of rather dense fibrin, thicker over the right lung than over the left. The pleural lining cells are usually quite well preserved; the pleural membrane much widened by œdema and by distention of the blood vessels. There are some hæmorrhages and a moderate infiltration with leucocytes and mononuclear wandering cells. The interlobular septa are wide and œdematous with a loose network of fibrin and a rather sparse infiltration with leucocytes and mononuclear cells. The latter are large and conspicuous with a rather abundant protoplasm about their deeply stained vesicular nuclei. No distinct granules are stained in the cytoplasm by the Wright or Giemsa stain and no definite mast cells are encountered. The lymphatics are wide and often filled with leucocytes and a network of fibrin. There are a few which seem to have in their walls a curious network of capillaries filled with blood and lying immediately under the endothelium.

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The bronchi are filled with a purulent exudate, their epithelium is well preserved and their walls are thickened only by œdema associated with a relatively slight infiltration of leucocytes. The alveoli are distended with an exudate which varies somewhat from place to place. In the more densely consolidated areas it is composed of closely packed polymorphonuclear leucocytes most of which are loaded with bacteria, so that they appear as little balls of organisms. Among them are relatively few red corpuscles, but there are many small mononuclear cells, such as have been described in preceding cases, with a finely granular neutrophile or acidophile cytoplasm and a deeply stained, solid, small, round nucleus. These are but slightly phagocytic for bacteria. There are also some of the larger mononuclears with relatively basophilic faintly granular or vacuolated protoplasm.

Fibrin is not especially abundant and is distributed in relation to changes in the alveolar walls. It seems that there is little evidence for Ribbert's view that bacteria are especially abundant toward the ductulus while fibrin is more abundantly produced in the marginal portions of the respiratory unit. In this lung, on the contrary, the formation of fibrin seems to be associated with thromboses of the capillaries of the alveolar walls. Most of the capillaries of the alveolar walls are intact and are evidently transporting fluid blood, but some in the network are plugged with hyaline fibrin thrombi. A surface view of an alveolar wall may show most of the channels open while one is thus obstructed, but in the commoner sectional view of the alveolar walls one sees either intact capillaries or a complete obstruction of the blood flow. From these thrombosed areas leucocytes are seen in process of emigration, while none actually appear to be entering the alveoli from the intact capillaries. From the hyaline fibrin thrombi there also radiates a network of fibrin in filaments into the alveolus (Figs. 14 and 15), so that one may expect to find, in the centre of the foci of fibrin, a stretch of thrombosed capillary. They are, however, so abundant that in some places the fibrin becomes a confluent network.

Examination of the exudate with various stains reveals a surprising condition, since with the Goodpasture-Weigert stain there are relatively few Gram-positive pneumococci to be seen. There are some, it is true, which are imperfectly stained or quite unstained, but still recognizable by their form, but the leucocytes are full of faintly stained Gram-negative coccoid forms. With the Giemsa, Wright or Wilson stain on the other hand, the intra-alveolar leucocytes are seen to be packed and loaded with well defined deeply stained, small, round cocci, so that, as stated above, many of them look like little balls of organisms. It is with such stains quite difficult to find the pneumococci, which can, however, be recognized by their form and their larger size. Occasionally large cells are found stretched along the alveolar wall loaded with these coccoid forms. In smears from the lung these Gram-negative cocci are very numerous, together with the pneumococci.

In Case 222 similar crowded coccus-like granules were seen and it was doubtful whether they were granules or organisms. Here it seems almost

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certain that they are organisms, although they were not recognized in cultures.

Case 230.—R. F. Onset on September 25, 1918, with general pains, fever, but no chills or cough. The patient was admitted to the hospital on September 29 with sore throat, dyspnœa and pain in the side. Cyanosis was marked. Eyes sunken, conjunctivæ inflamed; pain in right chest with bronchial breathing. Breath sounds exaggerated on left side. Delirium, deeper cyanosis and stertorous breathing. Temp. 100-104.6°. Pulse 108-160. Resp. 32-60. Died October 1, 1918, at 12.40. Autopsy four hours later.

Anatomical Diagnosis.—Bilateral confluent lobular pneumonia with fibrinous pleuritis. Ulceration of vocal cords.

Rectus muscles normal.

The *left pleura* contains about 5 c. c. of fluid with some floating fibrin. The surfaces are in general smooth and glistening, but there are some rough, prominent nodules in the posterior part of the lung.

The *right pleura* contains about 150 c. c. of turbid, brown fluid. The surfaces are dulled by an exudate of fibrin.

The *left lung* shows that the upper lobe is air-containing above and below, but in its central part shows several projecting nodules which are firm, dark red, flecked with hæmorrhage and rough on the surface. On section the upper lobe is air-containing except for these patches which show in the central part elevated lobules with red grey, dull, opaque surfaces surrounded by a hyperæmic, hæmorrhagic and more œdematous zone which slants down to the air-containing lung. Plugs of exudate project from the more solid central parts. In the lower lobe there is a patch of consolidation placed somewhat anteriorly, measuring about 5 cm. in diameter. The central part is grey and rough, the periphery red and œdematous. The bronchi are quite deeply reddened and their lining covered by a thin, greyish film.

The *right lung* is very large and heavy. The anterior part of the upper lobe is air-containing, but there is a large central area of consolidation which on section is found to be made up of a number of lobules which are rigidly consolidated with projecting plugs of exudate. Round about this for a rather wide area there is hyperæmia with œdema so that the tissue contains no air. The middle lobe is almost entirely consolidated and is very large. The lower lobe is completely consolidated except for a small paravertebral portion which contains air. On section the lower and middle lobes show irregular ramifying, elevated patches of consolidation which are dry, opaque and dark purple mottled with greyish red and flecked with projecting yellow plugs of exudate. Round this and less elevated, there is a marginal zone of greyish pink consolidation which is much smoother and which extends to the surface of the lung.

The organs of the neck are in general normal, but there are distinct minute ulcerations upon the edges of the vocal cords and an area of inflammation with grey, necrotic centre below the cord on the right side.

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Cultures show a Pneumococcus Type IV, in both lungs, right pleura, heart and pericardium, but in addition there were gram-positive bacilli in the lungs and Gram-negative bacilli in the pleura, heart's blood and pericardium. The nature of these bacilli does not appear. Sections from the larynx show large numbers of what appear to be Pfeiffer's influenza bacilli, together with staphylococci and large Gram-negative bacilli. Those from the lung show only pneumococci, but these in great numbers. Smears from the lung show typical pneumococci apparently in pure culture, so that it seems that the bacilli reported there in cultures must have been a contamination.

Microscopical Examination.—The pleura is not especially thickened, but is covered by a thin layer of fibrin with many red corpuscles. The interlobular septa are broadened by accumulations of fluid with fibrin and blood, together with abundant leucocytes and mononuclear wandering cells. The lymphatics are greatly dilated and are full of leucocytes often containing pneumococci and many mononuclear cells which act as phagocytes and enclose the bodies of leucocytes. These cells have pale vesicular nuclei and show no granules with Giemsa's stain. The bronchial walls are somewhat œdematous, but not especially infiltrated with cells. Their lymphatics are greatly distended with cellular exudate. The epithelium is low and flat, but it is continuous all around. The bronchi contain a purulent exudate in which pneumococci are the predominant organisms, but there are some leucocytes which contain small Gram-negative cocci. Indeed in some branches these are present in very great numbers so that nearly every leucocyte contains a few and some are packed with them. They are often arranged in pairs, sometimes in fours. It may be observed here that these Gram-negative cocci cannot be found in the alveoli although the pneumococci are present in very large numbers.

The consolidation of the lung substance varies in density. In some areas the alveoli are completely packed with masses of partly disintegrated leucocytes among which little blood and only scanty remains of mononuclear cells are found. Other areas are filled with an exudate made up almost entirely of blood with few leucocytes. About these areas there are zones in which the alveoli contain only fluid with a few leucocytes entangled in a network of fibrin. Pneumococci are present in enormous numbers in some places, closely packed in leucocytes and scattered free, while in other places they are less abundant and more diffusely scattered. The alveolar walls have in most places retained their epithelium. Where the exudate is most densely packed they are stretched out and narrow and seem to allow the passage of very few corpuscles. But in almost every part of the lung the alveolar capillaries are frequently plugged by a material which takes the fibrin stain and becomes continuous with radiating strands of fibrin which extend out into the alveoli. The circulation in the capillaries stops sharply at these hyaline thrombi. Leucocytes in these parts of the alveolar wall are distorted and appear to be emigrating or possibly moving into the injured area.

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Careful search for sources of hæmorrhage in the alveolar walls of those parts which are especially filled with blood shows no obvious breaks in the capillaries. Certainly one is not given the impression that any gross rupture of capillaries exists or that necrosis of the alveolar wall has occurred as has been suggested by several authors. Indeed, where, as in the thrombosed capillaries the injury seems greatest, there is no hæmorrhage.

The ulceration of the vocal cord is shallow but associated with much œdema of the underlying tissue. Various kinds of organisms are found in the ulcer, especially swarms of gram-negative cocci and small bacilli. There are few pneumococci.

AUTOPSY 5712.—K. C. C. Age 22 years. Admitted October 1, 1918. Had been sick five days. Onset with headache, general aching, malaise, fever and dry cough with slight expectoration. After admission to hospital profuse mucopurulent greenish sputum which became slightly blood-tinged. Bright red injection of larynx and palate. Slight dullness over right lower lobe with many râles. Spleen not enlarged. Temp. 104.2°. P. 100. Resp. 22. Leucocytes 3240. Died October 6, 1918. Autopsy two hours after death.

Anatomical Diagnosis.—Clinical history of influenza. Acute fibrinopurulent tracheo-bronchitis; confluent lobular pneumonia; bilateral fibrinous pleurisy.

Rectus muscles normal.

The *left pleura* contains 80 c. c. of cloudy fluid. There is a thin deposit of fibrin over the lateral and posterior surface of the lung.

The *right pleura* contains 30 c. c. of cloudy fluid. Surfaces slightly dull.

Left Lung.—Pleural surfaces roughened by thin deposit of fibrin. The lower and posterior half of the upper lobe almost completely consolidated. On section many large irregular areas show a greyish pink, finely granular surface, while between these areas the tissue is of a dark red color, airless but not firm.

Right Lung.—Pleural surface posteriorly has lost its gloss. The lower lobe is almost completely consolidated and rather firm. On section much greyish red purulent fluid covers the surface, which is dark red with a few small greyish red patches. Posterior and lower third of the upper lobe almost completely consolidated and also dark red on section. Middle lobe air-containing. Bronchi filled with a thin, blood-stained, turbid fluid. Their mucosa much congested.

The lymph glands at the hilum are large and soft and present some hæmorrhage. The trachea contains blood-stained turbid fluid. The mucosa is swollen and congested and its surface covered by a thin fibrinopurulent membrane. The tonsils are not altered.

Cultures from the blood, lungs and pleural fluid show Pneumococcus IV.

Microscopical Examination.—The pleura has lost some, if not all, of its covering cells, but there is no abundant layer of fibrin. The membrane is slightly œdematous and its lymphatics are distended with fluid loaded

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with pneumococci. The interlobular septa are very wide, their tissues spread apart by œdema. There are few cells to be found there, but in places great quantities of pneumococci. The bronchi have in places lost their epithelium. They are filled with fluid containing relatively few leucocytes except in areas of dense consolidation where they are numerous; but the lymphatics in their walls, as also in the walls of the blood-vessels and in the septa, are full of pneumococci. There is no especial dilatation of the ductuli alveolares. The alveoli are widely distended in places with fluid, elsewhere with a coagulated exudate composed of relatively few red corpuscles with many polymorphonuclear leucocytes and many small round mononuclear cells with a deeply stained solid-looking nucleus. In the œdematous areas the fluid is loaded with pneumococci. Very few leucocytes are gathered there. In the more densely consolidated parts the more numerous leucocytes are very actively phagocytic, but they are largely disintegrated or ragged. Pneumococci are not nearly so abundant in these areas and they appear to have become fragmented. On the other hand many of the leucocytes are loaded with small rounded Gram-negative coccus-like forms generally in pairs, sometimes in fours. These stain bright blue with Wilson's stain and are curiously infrequent outside of cells. Nothing corresponding with this grew in the cultures and this same observation applies to several other cases. The nature of these organisms—for from their morphology and behavior they seem to be bacteria—cannot be determined.

In some places the consolidation seems especially firm and there is a dense network of fibrin running through and filling the alveoli. In these places the capillaries in the alveolar walls contain a dense fibrin plug which extends to obstruct many of the channels in the alveolar walls. In other less intensely affected portions the capillaries are quite open.

GROUP 3.—*Cases in which a peculiar and characteristic pulmonary lesion is due to an overwhelming infection with Streptococcus hæmolyticus.*

CASE 219.—O. M. M. Onset on September 18, 1918, with headache, lightheadedness, pain in abdomen. The patient developed backache, cough and bloody expectoration, pains in chest, no nausea, vomiting or diarrhœa, no definite chills, but chilly sensations. Entered hospital September 23. Throat and conjunctivæ congested. Delirious. No physical examination made. Died September 28 at 6.25 p. m.

Blood Count.—	Leucocytes	Differential count Polym.	S. M.	L. M.	Tr.
September 23.....	7150	53	37	11	
September 26.....	10700	45	39	15	1 eos.

Autopsy 20 hours later.

Anatomical Diagnosis.—Confluent lobular pneumonia (right). Interstitial emphysema of lungs.

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The *left pleural cavity* contains about 100 c. c. of blood-stained fluid. The surfaces are smooth and glistening.

The *right pleural cavity* contains a similar amount of similar fluid. Its surfaces are also smooth and glistening, although there is some brownish stain and perhaps a few hæmorrhages on the diaphragmatic surface.

The *left lung* is voluminous, blood-stained in the posterior part, but everywhere air-containing. There is emphysema of the interlobular tissue. The bronchi are somewhat blood stained.

The *right lung* is very voluminous and heavy. Its interlobular septa are distended with gas bubbles especially along the anterior margins. The anterior part of the upper lobe is air-containing, the whole posterior part consolidated. The whole middle lobe and the anterior part of the lower lobe are air-containing, but the whole posterior part of the lower lobe is consolidated. On section the consolidated part of the upper lobe is almost black and uniform. It is difficult to see any outlines of the lobules or the alveolar marking. The lower lobe shows the wide interlobular septa distended with blood-stained fluid running across the lung. The area of consolidation is greyish brown in color and opaque, mottled with darker red. The consolidation is uniform, rather spongy and without conspicuous alveolar plugs. The bronchi are deeply blood-stained.

The other organs appear normal, although there is a general blood-staining which extends through the walls of veins to the surrounding tissue.

Cultures from lungs, pleura, heart's blood and spleen show Streptococcus hæmolyticus in pure culture.

Microscopical Examination.—The sections from the left lung are practically normal.

Those from the consolidated areas of the right lung show great swelling and infiltration of the pleural membrane in which the superficial layer is lifted away from the inner layer of elastic tissue by an accumulation of fluid which is loaded with tangled chains of streptococci. The interlobular septa are widened and œdematous with relatively few wandering cells, but great numbers of cocci. The whole tissue is necrotic with the exception of the walls of some of the larger blood-vessels and a few cells of the connective-tissue framework. It is all undisturbed as far as the position of the alveolar walls and other structures is concerned, but there is practically no nuclear staining. The bronchi contain a granular necrotic exudate composed chiefly of leucocytes and shadows of blood corpuscles, and loaded with streptococci. The walls have lost all their epithelium. They may be infiltrated with leucocytes which have become necrotic, but these are masked by the feltwork of streptococci which in many cases lines the lumen and extends into the lymphatics. The same is true of the walls of many blood-vessels in which the lymphatics are packed with streptococci.

The ductuli alveolares are not conspicuous and appear to contain leucocytes and blood. The alveoli are distended with an exudate composed of necrotic leucocytes, shadows of red corpuscles and very little fibrin. Their

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walls are, as already stated, practically quite necrotic. The capillaries contain occasional intact red corpuscles, but most of them are filled with a homogeneous hyaline material which appears to have resulted from the agglutination of red corpuscles. All the red corpuscles in the alveoli have been laked and the deep red color must have been due to staining of the necrotic tissue with hæmoglobin. The alveoli contain myriads of streptococci in chains. They are almost filled with a tangled network of these chains and in places are nearly solidly packed with this tangle. No other organisms are visible and search for the influenza bacillus gives no result.

The other organs show no especial abnormality except that streptococci in small masses are to be found in the substance of the spleen and of the adrenals and probably elsewhere. These masses are surrounded by necrotic tissue. Possibly the lapse of 20 hours between the time of death and the autopsy may have produced an increase in numbers of these organisms. The bone-marrow of the femur is almost entirely fatty with little evidence of hyperplasia.

Case 5720.—A. H. C. Aged 30 years. Onset on September 27, 1918, with chill, pain in the back and headache, prostration and fever. The next day the patient was much better and seemed well until October 3, when he had another severe chill and went to bed with a temperature of 104°. The throat felt raw and he had a slight cough. There was congestion of the pharynx and of the skin of the face and thorax. Leucocytes 4680. Slight impairment of resonance over right lower lobe on October 7; abundant râles on October 10, with suppression of breath sounds, cyanosis and delirium. On October 12 definite consolidation of the lower lobes. Leucocytes 10,200. On October 13 cyanosis and collapse. Temperature 102.2°. Died October 13. Autopsy three hours later.

Anatomical Diagnosis.—Confluent lobular pneumonia.

The *left pleural cavity* contains no excess of fluid. The surfaces are smooth and glistening.

The *right pleural cavity* contains 300 c. c. of blood-stained fluid. The surfaces are widely covered by an exudate of fibrin which binds together the lobes.

The *left lung* is smooth, superficially, and weighs 900 grams. It shows large areas of consolidation which are dense and dark greyish red where they show through the pleura. These are found especially in the lower portion of the upper lobe and the posterior portion of the lower lobe. On section the cut surface oozes a great amount of dark red fluid which contains no air. The more solid areas are not prominent and not very firm. The most striking feature lies in the presence of the extreme œdema.

The *right lung*, which is covered with fibrinous exudate, weighs 1900 grams and is very bulky and heavy. The consolidation is more widespread than in the left and occupies most of the posterior portion. On section these areas are firmer than the surrounding tissue, are dark red in color, and allow the escape of great quantities of dark red fluid. The intervening lung substance is also œdematous and almost airless.

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The *trachea* is definitely reddened and contains a red foamy fluid.

Cultures from the blood, lung, pleural fluid and pericardial fluid and trachea show Streptococcus hæmolyticus alone.

Microscopical Examination.—The sections of the lung show prominently an extraordinary œdema, an overwhelming number of streptococci and an almost complete necrosis of the tissue. The œdema thickens the pleura and the interlobular septa. The lymphatics are especially conspicuous by their great dilatation and the bronchial and vascular walls are spread apart. Even the alveolar walls are very thick, not from an infiltration of cells or new formation of tissue, but from an accumulation of fluid. The epithelium of the bronchi is in large part desquamated. The bronchioles, ductuli and alveoli contain a thick fluid which is coagulated on fixation in a coarse beaded network or in the form of a fine froth. It is rather refractive and takes a deep stain with eosin. There are relatively few leucocytes in the alveoli and most of these are loaded with streptococci. Many of them stain fairly well, although the epithelium of the alveolar walls is lost or necrotic and the walls themselves in many places show no nuclei or only pale shadows of the nuclei of connective-tissue cells. There is little blood in the exudate, but the walls of the alveoli are covered with a thick layer of bacteria which sometimes almost fill the cavity. The bronchi and lymphatics and even the substance of the tissue itself are all loaded with streptococci. No other organisms are seen.

Case 6134.—C. J. Aged 25 years. Had been in hospital for an operation for hypospadias since November 19, 1919. On January 16, 1920, the temperature began to rise with sore throat and cough. On January 24 the temperature was 104°, when evidences of bronchopneumonic consolidation were observed. On January 26 1800 c. c. of clear fluid were aspirated from the left thorax. On January 28 a large amount of pus was evacuated from the left pleura by thoracotomy. The patient died January 30. Autopsy ten hours after death. This was in the course of the epidemic of influenza and the clinical impression was influenza with empyema.

Anatomical Diagnosis.—Bilateral lobular pneumonia with unilateral empyema; congenital malformation of genito-urinary organs.

The *left pleura* contains 10 c. c. of fibrinopurulent exudate, and there is a thin purulent exudate covering the surface of the lung.

The *right pleura* is free from fluid and its serous surfaces are smooth and glistening.

Left Lung.—The upper lobe is air-containing except for a few firm areas in its lower portion. The lower lobe is almost entirely consolidated and firm. Its surface is covered by a thin purulent exudate. On section the cut surface of the upper lobe is normal in appearance except for circumscribed, red, elevated areas in its lower portion. On the cut surface of the lower lobe the bronchi are injected and filled with a fibrinopurulent exudate. Many of the small branches of the pulmonary vessels are filled with thrombi near the surface of the lung. The pulmonary tissue presents numerous almost confluent areas of consolidation which are greyish red, slightly elevated, rather dry and firm.

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The *right lung* is not so heavy as the left. Its surface is glistening everywhere and no consolidated areas can be felt in the two upper lobes. The lower lobe, however, is almost entirely consolidated and on section presents many red, elevated, circumscribed areas which contain no air and are definitely consolidated.

Cultures showed Streptococcus hæmolyticus in both lungs.

Microscopical Examination.—The sections take a very faint stain and the tissue is found to be very soft and easily disintegrated. The pleura looks dull without overlying layer of fibrin, but is infiltrated with bacteria. The interlobular septa are in general not wide, but the lymphatics are very greatly distended with leucocytes and bacteria. This is true wherever they are found. The bronchi have lost their mucosa and are lined or rather filled with a necrotic and fibrinous mass loaded with bacteria. They and the blood-vessels seem fairly isolated by the enormous dilated lymphatics in their walls. The alveoli are collapsed or distended with fluid. Their walls are indefinite in outline with only an occasional faintly staining nucleus. In whole areas the tissue is practically completely necrotic. There is little cell exudate, a few leucocytes and desquamated epithelial cells with ragged shreds of fibrin, and there is no characteristic dilatation of the ductuli. The alveolar spaces contain chiefly a fluid which in places seems gelatinous and thick, because it coagulates on fixation into a dense pink-staining material. Elsewhere it assumes a granular and reticular form. Everywhere there is a little hæmorrhage and since so many of the alveoli contain no red corpuscles it may be suspected that the density and pink staining of the fluid are partly due to hæmolysis.

Streptococci in tangled clumps of long chains are present everywhere, apparently in unmixed culture. They float free in the fluid in the alveoli or are massed together in the lymphatics and in the bronchi.

CASE 6142.—K. M. Aged 29 years. Onset on February 4, 1920, with general malaise, coryza and slight cough, aching pains in joints and muscles. On February 6 severe pain in right chest with dyspnœa; severe chills, high fever and blood-tinged stools. Brought into the hospital *in extremis*. Temp. 104°. P. 160. Resp. 60. Leucocytes 7400. Dyspnœa, cough, expectoration of bloody, frothy fluid. Severe abdominal pain and deep cyanosis. Blood-stained fluid discharged from the nose, and the mouth and pharynx are filled with frothy blood as the patient breathes. Death February 8. Autopsy 23 hours later.

Anatomical Diagnosis.—Acute confluent lobular pneumonia with œdema and generalized blood-staining.

The *left pleura* contains about 150 c. c. of fluid which looks like almost pure blood. The surfaces are roughened by old adhesions.

The *right pleura* is also partly obliterated by old adhesions and contains 200 c. c. of fluid which looks like pure blood. The pericardial cavity contains 200 c. c. of blood-stained fluid.

The *left lung* is wet, easily torn, and most of it can be incompletely blown up with air. On section the cut surface about the bronchi is very

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œdematous. In the upper as well as the lower lobe the bronchi are deeply reddened and contain frothy fluid. The tissue is blood-stained about all the larger vessels. The uppermost part of the upper lobe is easily distended with air. The lower part is dark red and appears to be loosely consolidated. In the lower lobe the cut surface is in general smooth and there are patches throughout which can be distended with air, but there are also patches which are greyish red in contrast to the bright red, air-containing portion. They are not roughened and seem to contain a little air, but are firmer than the surrounding tissue. There are, therefore, no definite rigid areas of consolidation, but only a diffuse œdema with blood-staining, and a partial consolidation.

The *right lung* is almost entirely covered with adhesions in the anterior portion. The posterior surface is deep purple, œdematous looking, but smooth. There are no definite hæmorrhages on the surface, but there are a few between the lobes. The posterior part of both lobes is heavy and boggy, as though filled with fluid. The interlobular septa are conspicuous as deeply blood-stained lines. On section the posterior part of the upper lobe is dark red and very moist, in these respects contrasting with the dry, paler, air-containing anterior part. The dark red tissue is elastic, quite satiny and smooth on section, but oozes a bloody fluid. In the lower lobe the bronchi are dark red, containing a frothy fluid. The lung substance apparently contains a little air since there are small pale areas scattered about, but in general it is deep red in color and the cut surface nowhere roughened. The bronchial glands are very moist, but are not enlarged.

Cultures from the heart's blood, lungs, pleural cavities, trachea and from the pharynx show Streptococcus hæmolyticus. The influenza bacillus is associated with this in the lungs, trachea and pharynx, and in the trachea there is also Staphylococcus aureus.

Microscopical Examination.—The pleura shows no fibrinous exudate, but is thrown up into wrinkles and much thickened. The interlobular septa are not especially conspicuous, but the adventitial walls of the bronchi and blood vessels are enormously widened by œdema.

The bronchi have lost their epithelium and the underlying tissue is œdematous with a hyaline thickening of the basement membrane. The ductuli are not dilated. The alveolar walls are everywhere practically necrotic in that all the epithelium has disappeared, and while the outlines of the capillaries can generally be distinguished, relatively few nuclei take any stain and those stain but palely. The alveoli are all filled with granular coagulated fluid practically altogether without cells except for a few partly laked red corpuscles and some debris of epithelium. The blood in the capillaries and smaller venules appears disintegrated or in shadow form. All the œdematous tissue and the fluid in the alveoli and bronchi are loaded with streptococci. The thickened pleura is densely packed with them. Mixed with the streptococci are large, stout, Gram-positive bacilli in considerable numbers. The part played by these in producing the necrosis and hæmolysis is uncertain, and since they failed to grow in the

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cultures it is difficult or impossible to say what they are. It appears, however, from analogy with other cases of streptococcus infection that the destructive effects were essentially due to the streptococci.

In these four cases there is no confusion about the nature of the bacterial invasion since cultures, smears and sections show in overwhelming numbers *Streptococcus hæmolyticus* without any other organisms. The anatomical changes are so much alike and so peculiar that it seems fairly safe to assume that this is the characteristic result of the invasion of the hæmolytic streptococcus in the lungs of persons ill with influenza. Something resembling this in a slight degree was found in a few cases in the previous epidemic of measles in which so many died of a pneumonia caused by a secondary invasion of the hæmolytic streptococcus, but in that epidemic most of the cases presented an interstitial bronchopneumonia in which peribronchial interstitial infiltration and new formation of tissue prevailed. It was only in a small number of cases, which were thought to be instances in which resistance to bacterial invasion was very much lowered, that we found the streptococci growing abundantly and freely throughout the lung tissue, causing necrosis and hæmorrhage with laking of blood and with little sign of protective reaction.

But in none of these instances did the intensity of the infection or its consequences approach what is seen in such cases as the four described above. It can perhaps be taken to mean that although measles predisposes to invasion of the hæmolytic streptococcus, influenza annihilates the resistance of the individual so that when he is exposed to infection with the hæmolytic streptococcus his tissues act almost like an inert culture medium in which a colossal growth of these cocci in chains occurs with such rapidity that the tissues are simply killed, flooded with blood and fluid and stained with the hæmoglobin from the laked blood. One of these patients was actually working with great quantities of the hæmolytic streptococcus in the laboratory and it is conceivable that his infection may have been imminent all through the summer but that while well he resisted the organisms, whereas the infection came on at once in full force when his resistance was destroyed by the attack of influenza.

In all instances the throat and pharynx were reddened and sore and much frothy fluid stained with blood was coughed up. At autopsy the explanation of this is found in the extreme œdema of the lungs. The pleural cavities are filled with a deeply blood-stained fluid. The

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whole lung tissue is distended with blood-tinged fluid so that the lymphatics stand out as dilated channels of red fluid. The consolidation is relatively inconspicuous in the presence of this enormous œdema. Microscopically, there is little exudate of cells or fibrin but every part of the tissue is profoundly injured. The bronchi are denuded of epithelium, œdematous and loaded with tangled chains of cocci both in their walls and in their lumina. The alveolar walls are necrotic, the epithelium desquamated and their cavities full of thick blood-stained fluid with only the debris of laked red corpuscles and a few leucocytes, among which lie the chains of streptococci often so numerous as to form a sort of feltwork. There is no dilatation of the ductuli with hyaline lining. If it ever existed it has been masked completely by the effects of the streptococci.

On the whole it seems that this type of pneumonic reaction is quite peculiar and specific so that it is very easily recognized. Since it must depend upon an extreme disturbance of the balance between the power of resistance of the body and the virulence of the streptococci, it is probable that it will not be seen again until another epidemic of influenza occurs.

In the previous paper already mentioned,* a description of the lesions found in the lungs of those who had developed pneumonia after influenza, in which the influenza bacillus of Pfeiffer was found in pure culture or as the predominant organism, was based on the study of a number of cases in which the duration of the illness averaged about nineteen days. These will be described in detail below and it will be found that they present very uniform and specific characteristics. But there are certain other cases in which it seems probable that the bacillus of Pfeiffer is the predominant organism, but which are very different in some ways from these, possibly because in them the duration of the whole illness averaged only about thirteen days. In them, as the following case records will show, there is profuse hæmorrhage which tends to mask the bronchial infiltration and even to cover up the patchy character of the inflammatory reaction. It is rather difficult, though not impossible, to believe, however, that the prolongation of the illness by another week could cause the complete disappearance of all this hæmorrhage with the appearance of the nodular peribronchial

* Jour. Amer. Med. Assoc., 1919, LXXII, 720.

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induration which is so striking in the group of cases to be described later. There is one case in the series described in a previous paper on the pneumonias associated with measles which appears to belong in this group. In Case 192, at Camp Dodge, there was no history of measles but influenza bacilli were found in great numbers associated with profuse hæmorrhage and a peribronchial infiltration.

GROUP 4.—*Cases in which the Bacillus influenzæ is predominant or in pure culture. A: Acute peribronchial infiltration accompanied by extensive hæmorrhage and œdema.*

CASE 214.—D. S. Onset on September 14, 1918, with backache, headache, malaise, chills, fever and cough. Abdominal pains, epistaxis. Temp. 104°. P. 80. Resp. 20. The patient entered the hospital on September 22, with dyspnœa, conjunctivæ injected, lips dry and cyanotic, throat injected, tonsils swollen. No jaundice. Dullness and râles over the left upper chest, anteriorly and posteriorly. On the right side tactile fremitus increased, dullness and râles in upper axillary region. Cyanosis of lips and fingers continued. Breathing rapid, shallow and labored. Died September 27. Leucocytes, September 24, 5500. Polymorphonuclears 66%. Lymphocytes 22 Leucocytes, September 27, 7850. Polymorphonuclears 80%. Lymphocytes 15

Autopsy September 28, 21 hours after death.

Anatomical Diagnosis.—Confluent lobular pneumonia.

The *left pleural cavity* contains 80 c. c. of slightly turbid brown fluid. The surfaces in general are shining, but not quite smooth. They are deep purple with patches of brick-red stain over the lower part of the upper lobe and posterior part of the lower lobe, also over the diaphragmatic and mesial surfaces.

The *right pleural cavity* contains only about 20 c. c. of brownish fluid. The pleural surfaces are smooth and shiny, but flecked with hæmorrhages with the same dull red patches especially on the outer and diaphragmatic surfaces of the lower lobe.

In the upper lobe of the *left lung* (Fig. 16) the apical and anterior portions are air-containing and normal looking. The whole lower and posterior part is occupied by an area of consolidation which is dark greyish red in color and not very prominent above the surrounding cut surfaces. The lung still has a spongy structure and no definite plugs are seen in the alveoli. The marginal portions of the area of consolidation are intensely hæmorrhagic. The framework of the lung is unaltered and the bronchi are not deeply reddened. In the lower lobe the upper and lower edges are still air-containing, but nearly all the rest is consolidated. The cut surface of this area is not much elevated above the air-containing lung. It is not opaque grey, but rather spongy and dark greyish red. No distinct alveolar plugs are visible. On the contrary the lung substance looks as though each alveolus were extremely thick-walled, forming a dense spongy mass. Some portions of this are much more densely mottled with hæmorrhage

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than others and there are a few minute branched opaque yellow foci which may represent small bronchioles. The bronchi, interlobular septa and blood-vessels are scarcely changed. The bronchial glands are large and moist.

The upper lobe of the *right lung* is air-containing except for two small areas near the anterior margin, and the middle lobe similar except for small areas which occupy three or four lobules. These are rather pale on section. The lower lobe is heavy, flabby, not hard, deep purple in color, flecked with hæmorrhages and covered with a network of distended lymphatics. It has not the rigidity belonging to lobar pneumonia, but is more flabby. On section it shows a large area of consolidation like that in the left. It is dark greyish red with patches of darker red, and close examination fails to show individual plugs in the alveoli. The lung is coarsely spongy. The bronchi, including the main bronchus, are but slightly reddened and contain a frothy fluid which is not opaque even when squeezed from the consolidated area.

Microscopical Examination.—Part of the tissue of the lung was fixed in alcohol, part in Zenker's solution, so that the sections taken from the alcohol tissue have the advantage of revealing what is left when the red corpuscles are reduced to shadows and incapable of staining. There is such extensive hæmorrhage that in the Zenker tissue, in which the red corpuscles are well preserved, nearly everything is covered and masked by the blood. The character of the lesions is fairly uniform throughout. The pleura is scarcely altered except by the infiltration of blood corpuscles in certain areas. The interlobular septa are slightly widened and the lymphatics are dilated and partly filled with leucocytes.

The bronchi and bronchioles are very markedly affected, as is especially apparent in the alcohol tissues. They are loosely filled in places with leucocytes, in other places they contain only a few cells. In these leucocytes are found quite abundant minute Gram-negative bacilli, which must be influenza bacilli in view of the cultures from the lung which showed exclusively that organism. The epithelium is generally intact or lifted up from the underlying tissue. The walls of the bronchioles are thickened by œdema and great dilatation of the blood vessels together with infiltration by mononuclear and other cells so that they look like granulation tissue. This change extends to very small bronchioles, but does not affect the walls of the adjacent alveoli which are thin. Most of the ductuli alveolares contain fluid with some red corpuscles and a few leucocytes. The alveoli themselves show no especial change in their walls except the desquamation of some epithelial cells. They contain chiefly red blood-corpuscles in great numbers, but there are many which are occupied entirely or through half of their diameter by fluid. There is in most a delicate network of fibrin and a few mononuclear wandering cells and polymorphonuclear leucocytes. There is no dense accumulation of these cells, however, and in the alcohol tissue the alveoli appear in section very empty of nucleated cells and chiefly filled with coagulable

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fluid and red corpuscles. In this respect they contrast with the terminal bronchioles which are often full of deeply stained leucocytes and are conspicuous from the changes in their walls. In the neighborhood of some bronchi the alveolar cavities show a thick lining of deeply stained hyperplastic epithelium which stands out prominently, but otherwise the changes in the alveoli and even in the terminal ductuli alveolares seem very acute. Prolonged search for bacteria in the contents of the alveoli revealed only one or two and those in the immediate neighborhood of bronchioles. In the contents of the bronchioles themselves, however, the influenza bacilli are quite numerous.

The *spleen* presents no gross alteration, but microscopically a rather remarkable accumulation of myeloid cells in the pulp about the Malpighian bodies is observed.

The *bone-marrow* from the femur is almost entirely composed of fat. The *rectus abdominis* muscle shows no hyaline degeneration, but contains trichinæ.

Cultures gave B. influenzæ from both lungs, but not from the pleuræ. Those from the heart's blood, spleen and pericardium were sterile. From the sphenoid sinus, which contained turbid fluid, Staphylococcus albus and B. influenzæ were recovered.

Case 215.—D. G. Onset on September 18, 1918, with headache, fever, chills, malaise, cough, expectoration, pain in chest and weakness. Temp. 103.8°, pulse 98, resp. 26. He was given triple vaccine on September 8, after which he had had coryza, epistaxis and headache.

Admitted to hospital September 21, coughing, drowsy, with pain in abdomen, chest and back. Cyanosis of lips with slight jaundice. Tonsils slightly enlarged. On the left side dullness from apex of lung to 2d interspace. On the right expansion was limited and there were dullness and bronchial breathing from the third rib down with crackling râles. Blood pressure 98.54. Died September 28, 1918. Autopsy five hours later.

Anatomical Diagnosis.—Bilateral confluent bronchopneumonia with scattered peribronchial infiltration. Fibrinopurulent pleuritis (right). *Ulceration of vocal cords.*

The *left pleural cavity* contains no excess of fluid. Its surfaces are slightly roughened and over the posterior part are covered with an exudate of fibrin.

The surfaces of the *right pleura* are everywhere covered with a thick honeycombed layer of yellow fibrin except over the anterior part of the apex. The cavity contains 300 c. c. of turbid fluid with floating shreds of fibrin.

In the *left lung* the bronchi exude a thick brownish gelatinous fluid. The bronchial glands are large and moist. The upper lobe is almost everywhere air-containing, but a few firm nodules are felt. The surface of the lower part of the upper lobe and that of the lower lobe are roughened by fresh fibrin and flecked with numerous hæmorrhages. There are some firm nodules in the lower lobe, especially at the upper and lower margins.

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On section the lung shows in the upper lobe normal air-containing tissue with a few small projecting nodules. In the posterior part of the lobe the bronchi become conspicuous by being surrounded by hæmorrhages. In the lower lobe a few lobules are distinctly consolidated. In these the greater part is occupied by dark red hæmorrhagic tissue, but there are several small groups of grey nodules scattered throughout. In the more posterior part there are bronchi which are slightly thickened, deeply reddened and lined with a dull opaque shreddy membrane. The tissue surrounding these bronchi is hæmorrhagic and there are clustered round them numerous small areas of consolidation measuring nearly 2 mm. in diameter. The terminal portions are thickly surrounded by clusters of groups of consolidated alveoli, but the intervening lung tissue is air-containing.

In the *right lung* the upper lobe is air-containing except for an area of consolidation in the lower mesial part. The middle lobe shows an area of uniform consolidation near the upper surface, while in the lower lobe the whole upper and posterior part is consolidated. On section the areas of consolidation in the upper and middle lobe are greyish red with an obvious intra-alveolar exudate. In the middle lobe posteriorly there is a small grey softened area from which the tissue has fallen out. A bronchus leads directly into it. The remainder of the tissue is thickly studded with opaque yellowish white areas which seem to correspond with the bronchi.

The lower lobe is more uniformly consolidated, especially in the posterior portion, but even this consolidation is not quite uniform, being mottled with yellow and dark red areas. Its surface is uneven. The bronchi are very deeply reddened and contain a thick yellow pus. Their walls are lined with an opaque greyish material.

On the whole the right lung shows in both upper and lower lobes, especially in their posterior portions, large areas of consolidation which are fairly homogeneous, although showing flecks of yellowish opacity. In the middle lobe these flecks are distinctly peribronchial and the consolidation is far from homogeneous. The bronchial glands are very large, deep red and moist.

The vocal cords show a slight loss of substance along their margins. The rest of the larynx is pale, as is also the trachea down to the bifurcation where it becomes deeply reddened with superficial erosions.

Cultures taken at the autopsy show from both lungs a gram-negative coccus, a mucoid pneumococcus and Gram-negative bacilli. The pneumococcus is also found in cultures from the heart's blood.

Microscopical Examination.—The lungs in different areas show a rather extraordinary variety of changes.

Sections from the *left lung* show in some cases a pleura over which the lining cells are still present, although the pleural membrane itself is filled with blood in places and with leucocytes in others. In other places it is covered with fibrin. In those areas under which the consolidation is only peribronchial the interlobular septa are little changed and most of

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the lung substance is air-containing. But there are small foci involving the terminations of the bronchi which stand out sharply from the surrounding air-containing tissue. The bronchioles are full of a purulent exudate, the epithelium partly desquamated, the wall moderately or intensely infiltrated with leucocytes. The surrounding alveoli are filled with blood and leucocytes which infiltrate also the walls of the alveoli. In places such peribronchial areas are larger and so numerous as to be almost confluent. In these foci one wall of the bronchus is usually completely replaced by a mass of fibrin and leucocytes which has displaced the epithelium, while the lining is intact on the other side. There is no definite organization nor any induration of the tissue.

In the *right lung* there are much larger and denser areas of consolidation. The pleura is thickly covered with fibrin and is itself densely infiltrated with leucocytes and red corpuscles. The interlobular septa are greatly thickened and œdematous with closely packed leucocytes and mononuclear wandering cells. The lymphatics are enormously dilated and distended with leucocytes and fibrin, and great numbers of pneumococci are present. In places there are abscess-like accumulations of these cells which seem to have arisen from lymphatics.

The bronchi are filled with leucocytes, often with an admixture of blood. Their epithelium is often well preserved, but in many cases desquamated. The walls of the smaller ones are infiltrated with leucocytes. The blood vessels show a similar infiltration with leucocytes which in many places lift up their endothelium by accumulating beneath it in a thick layer.

The consolidation of the lung itself is rather patchy inasmuch as the character of the exudate varies from place to place. In some areas it is intensely hæmorrhagic, in others there is no blood in the alveoli, but only leucocytes. In these latter areas the alveoli are greatly distended, the leucocytes not closely packed, but throughout whole areas necrotic. The alveolar walls are stretched, but their capillaries are full of blood except where they pass through particularly dense necrotic exudate. There it is plain that some of the walls are quite necrotic and coagulated, without, however, giving rise to any hæmorrhage. Indeed it seems that this would act as a protection against hæmorrhage. Other areas show a very densely packed leucocytic exudate with little fibrin except in certain alveoli where it is dense and closely packed. Some alveoli are filled with blood. In other areas desquamated cells become a prominent feature. But in most of these areas the alveolar walls and framework of the lung in general are but little altered. The epithelial lining cells are largely recognizable and in most places there is only slight infiltration of the walls. In some areas, on the contrary, the alveolar walls appear as shaggy strands of stretching and wandering leucocytes. No organization of the exudate occurs.

On the whole it is a pneumonic exudate, hæmorrhagic in places with infiltration of the interlobular septa, bronchial walls, blood-vessel walls and even alveolar walls with leucocytes but not with mononuclear cells

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and not associated with organization or induration. It is in part prominently peribronchial, but this characteristic is not maintained.

In sections stained to show bacteria a great variety of organisms are found. The bronchial contents show especially large gram-negative cocci mostly in leucocytes, swarms of influenza bacilli also chiefly in cells, other swarms of pneumococci which are chiefly free, Gram-positive organisms, which may be pneumococci but which show very distinct polar staining, and rather numerous very large gram-positive bacilli. In the alveoli the pneumococci and large bacilli are most abundant, the influenza bacilli and cocci being rarely found.

Case 220.—T. B. Entered Camp Lee September 4, 1918. Had had a slight cold before entry. Onset on September 14 with headache, chills, fever, dry cough, general aching and a tired, drowsy feeling. No epistaxis. No nausea nor vomiting. Some pain in abdomen. Anti-typhoid vaccine on September 7 with no reaction. Admitted to hospital September 20. On September 25 general weakness, fever, chills, etc. Râles over both lungs with dullness in the left axilla. Tactile fremitus increased over left side. Bronchial breathing over angle of scapula on left. Temp. 98-99.6°. Pulse 56-88. Resp. 20-26.

Blood Count.—		Differential count			
	Leucocytes	Polym.	S. M.	L. M.	Tr.
September 25	3150	58	26	16	
September 26	7750	54	33	13	

Doing well until September 29 at 10 p. m., when he suddenly broke out into a cold sweat. Pulse increased from 56 to 140. Not delirious. Respiration labored, cyanosis. Died September 29, 1918, at 10.35 p. m. Autopsy 11 hours after death.

Anatomical Diagnosis.—Bilateral lobular pneumonia, disseminated tubercles of lung, liver, spleen and bronchial glands. Hyperplasia of bone-marrow.

The *left pleural cavity* contains no fluid. Surfaces smooth and glistening.

The *right pleural cavity* contains no fluid. Surfaces glistening.

Left Lung.—The surface is smooth except for a retracted scar in the apical portion posteriorly. There are several firm, dark purple masses in the lower lobe, none in the upper. On section the upper lobe is in general air-containing, but contains a few areas of consolidation. The lower lobe shows numerous small scattered areas of deep red with a greyish center. These are often clustered around the ends of the bronchi. In the lowermost part there is a large area which is spongy, but elevated and fairly firm and made up of confluent reddish black patches which are studded with numerous yellow opacities. Anteriorly there are numerous minute and discrete hæmorrhagic foci. The bronchi are not especially reddened and contain only frothy fluid. The bronchial lymph glands are all large, even deep within the lung.

The *right lung* (Fig. 1) is very voluminous and air-containing almost everywhere, but there are large scattered patches of deep purple consolida-

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tion in the posterior part of the upper and lower lobes. On section the upper lobe shows only a few small patches of spongy dark purple consolidation. The lower lobe shows a more extensive group of the same small elevated almost nodular peribronchial clusters of consolidated tissue. These are grey in the center and dark red in the periphery. There are some large patches occupying lobules and sharply outlined which are dark purple and rather homogeneous, although also containing opaque grey spots. In the more posterior parts of both upper and lower lobe there are deep purple patches of consolidation irregular in outline. These are sometimes sharply outlined by the interlobular septa, and there it is seen that they contain small central greyish flecks. The middle lobe shows little evidence of consolidation. The bronchi are filled with opaque yellow mucus.

The *liver* and *spleen* contain scattered opaque yellowish nodules which resemble tubercles.

The tongue, uvula, tonsils, pyriform sinuses, epiglottis, vocal cords and trachea appear normal.

The *frontal sinuses* contain a slightly turbid fluid, but the mucosa is not injected and seems normal. The sphenoid sinus contains a thick yellow mucopurulent fluid. The middle ear and mastoid cells are normal.

The bone-marrow of the femur is light chocolate brown and firm.

Cultures from the lungs were sterile. Smears from the cut surface showed no bacteria. Cultures from the spleen, nasal sinuses and pericardium were also sterile, but that from the heart developed a few colonies of Pneumococcus Type IV.

Microscopical Examination.—The sections of the lung present a most peculiar appearance in that there is rather extensive thickening of the bronchial walls and general interstitial infiltration, together with much evidence of the organization of exudate in bronchioles and alveoli, while at the same time there is a profuse hæmorrhage which fills the bronchioles and alveoli with fresh red corpuscles. This is not unlike the streptococcal interstitial bronchopneumonia, but most diligent search of many stained sections fails to show any bacteria at all and smears and cultures were equally negative. One is forced to the conclusion that it is not so fresh a condition as was thought, but that the exudation of red corpuscles has begun afresh. There are but few areas in which the alveoli contain an exudate of leucocytes, and in these, too, bacteria are searched for in vain. The pleura is somewhat thickened and the interlobular septa are very markedly so, being infiltrated with wandering cells, chiefly of mononuclear types, with fluid and a network of fibrin and with some blood.

The bronchioles contain an exudate which is in places rich in leucocytes, many of which are becoming disintegrated. With these there is much blood. The walls form a thick layer of very vascular granulation tissue from which most of the epithelium has dropped off. This granulation tissue is densely infiltrated with mononuclear cells. The alveolar walls are in certain quite large areas perfectly normal and the alveoli are empty. In most places, however, they are thickened, showing sometimes many wandering mononuclears. Their epithelium is partly desquamated, but

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partly increased in thickness and depth of staining so that it becomes a most conspicuous thick, deeply colored lining layer. The alveoli throughout such areas usually contain a broad loose strand of connective tissue which is covered with epithelium; or else they are filled with a spongy network of connective tissue over some strands of which the epithelial cells have grown. Aside from these evidences of organization of a former exudate, there is nothing there—or the remaining space may be filled with fresh red corpuscles. Whole patches show every alveolus full of blood. There are certain areas in which the alveoli contain a dense exudate of leucocytes partly disintegrated and not accompanied by much blood.

In none of these localities, nor even in the coagulum which is frequently found in the lymphatics in the bronchial walls, could any bacteria be discovered.

It is conceivable that this may be the anatomical change characteristic of the epidemic disease influenza alone when not complicated by a secondary bacterial infection, but this seems unlikely for several reasons, and the rather obvious alternative is that it is a case in which after the lapse of a considerable period of time the bacteria have been destroyed and the exudate organized. This fails, however, to explain the terminal lesion with its extensive hæmorrhage.

The other organs show no special alterations, although the mucosæ of the nasal sinuses are much inflamed and infiltrated with mononuclear cells and a few leucocytes. No bacteria are found there either. The rectus abdominis muscle shows a few scattered hyaline fibres in which the clumps of hyaline material are surrounded by clusters of nuclei. The bone-marrow is in a state of advanced hyperplasia.

It will be observed that of these three cases only Case 214 showed the bacillus of Pfeiffer clearly in cultures and sections and without the admixture of other organisms. Case 215 shows them present in clouds but there are also several other organisms of which it seems probable that the pneumococci at least were active in modifying the lesion. In Case 220 we have a lesion identical with that in Case 214 and in Case 192 of the Camp Dodge series, but without finding by cultures, smears, or sections any organisms of any kind. If we include Case 192 we have four cases, in three of which the bacillus of Pfeiffer was present in great numbers and in all of which the lesion appears to consist essentially of an intense injury to the walls of the bronchioles with loss of their epithelium and infiltration of the tissue of their walls and those of the adjacent vessels and occasionally of the alveoli. This bronchiolar and peribronchiolar affection becomes conspicuous if we wash away the blood which submerges everything. Otherwise, the whole tissue appears filled and stretched apart by hæmorrhage. Organization of the exudate has definitely begun in Case 220, which had lasted

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fifteen days, but there is no trace of it in Cases 214 and 215, which had lasted thirteen and ten days respectively.

It is the peribronchial character of this lesion which constitutes its close analogy with the change in the group which is to follow, and the finding of one such case in which the bacillus of Pfeiffer is present in pure culture, which inclines us to the belief that this hæmorrhagic lesion represents the more acute form of the effect of the influenza bacillus upon the lung.

In these cases the lungs are distended, covered with a thin exudate of fibrin or with patchy areas of hæmorrhage, the bronchi exude a blood-stained or brownish frothy fluid, and on section the whole cut surface, or large areas of it, is deeply hæmorrhagic and moist with focal greyish opacities round the bronchioles, or else the hæmorrhagic consolidation is limited to numerous small patches about the bronchioles. Some of these lungs have been more intensely bloody than any of the forms produced by other organisms.

GROUP 4.—*Cases in which Bacillus influenzæ is predominant or in pure culture. B: Cases in which the slow course leads to the production of hard, nodular, peribronchial interstitial infiltrations of the tissue and exudation into the alveoli and bronchi.*

CASE 80.—R. J. S. Onset on September 26, 1918, with cough and pain in the left side. Admitted to hospital September 29 with soreness in chest and abdomen, congestion of pharynx and fever. On September 30 there was dulness over the right base, crepitant râles in the right axilla and over the left base. Temp. 102-98°. Pulse 96-106. Resp. 22-36. Died October 11. Autopsy three hours after death.

Anatomical Diagnosis.—Bilateral interstitial bronchopneumonia with organization. Embolism of pulmonary artery. Hyaline degeneration of rectus abdominis with hæmorrhage.

The *right rectus muscle* shows a hæmorrhage which extends from about the middle into the lower portion. On the left side the lower portion of the muscle is very pale, almost white, but there is very little hæmorrhage.

The *left pleura* contains no excess of fluid; its surfaces are everywhere glistening.

The *right pleura* contains no fluid. The surfaces are everywhere glistening.

The *pulmonary artery* contains a large mass of thrombi which extends into both branches, plugging them completely. Search in the femoral veins and elsewhere failed to reveal the source of these emboli.

The *left lung* is rather voluminous and both upper and lower lobes are in part air-containing, but they present also rather large, firm nodules embedded in the tissue. The bronchial nodes are enlarged and grey. The

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bronchi are pale and contain a small quantity of sticky purulent exudate.

On section the upper lobe is largely air-containing, but there is in its central part an elevated, sharply outlined mass, about 4 cm. in diameter, which is grey, nodular and translucent. There are other nodules of exactly the same character in the anterior part of the lobe. They are very sharply outlined, not hyperæmic and quite unlike the usual areas of consolidation in that the firm tissue itself cuts smoothly and is dense, homogeneous, elastic and far from opaque. In the lower lobe there are many similar areas.

The *right lung* is voluminous. The upper lobe contains a solid area at the extreme apex and many other firm nodules in other parts. So, too, the middle and lower lobes are studded with firm masses. On section these have in all cases the same grey, translucent appearance as in those of the left lung. The cut surface is smooth and the tissue elastic. The bronchi contain a purulent exudate and appear opaque where they are seen within the areas of consolidation. Some of these areas in the lower lobe are darker in color and flecked with hæmorrhage.

Cultures from the lungs gave growths of Pfeiffer's influenza bacillus together with some colonies of Staphylococcus aureus. Those from the trachea showed the influenza bacillus, Staphylococcus albus and aureus and a pneumococcus.

Microscopical Examination.—Sections from the apical and other areas of consolidation of the right lung and those from the left show the same condition. The pleura is not especially thickened or changed in any way except over those solid areas which reach it. There the lining cells become cubical and are often overlaid by a kind of dense cellular granulation tissue. The interlobular septa, too, are normal except where they are directly associated with one of the areas of consolidation when they are broadened by a great increase in new connective-tissue cells and infiltrated with mononuclear wandering cells, but not with fluid or fibrin. The consolidated areas surround bronchioles and are really broad zones in which the whole framework of the lung is greatly fortified by new tissue, while the alveolar cavities are filled sometimes with an exudate, but far more often by masses of newly formed connective tissue completely covered with epithelium. The bronchi are filled with polymorphonuclear leucocytes which in most instances contain a few influenza bacilli. There are some Gram-positive staphylococci present too. Both of these organisms are also to be found among the leucocytes which fill some of the alveoli. The bronchial epithelium is usually intact and is high and columnar, often in several layers. There are places, however, in which it has disappeared over a part of a bronchial wall and this area has become covered with fibrin which extends out into the bronchus; or if it has already become organized, the denuded patch of bronchial wall forms the starting point for a column of new connective tissue which may extend, branching out into the distal alveoli. The bronchial walls are slightly thickened, partly by the accumulation of plasma cells and other mononuclear wandering cells, partly by a new formation of connective tissue. Occasionally leucocytes

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are found burrowing under the epithelium, and the lymphatics often contain leucocytes.

The alveoli in some cases appear filled with leucocytes, others are full of blood, but in most cases the exudate appears much older, so that few cells remain and the mass of fibrin has become compact and densely stained. Such cells as appear within and about these masses are usually mononuclear cells and some of them are desquamated epithelium. But in general the alveolar contents are transformed into masses of new connective tissue with blood-vessels, and covered by new formed, high cubical epithelium. Such masses are often attached here and there to the walls and their connective-tissue filaments are continuous with those of the wall, but it is clear that they extend into other alveoli and probably into the bronchi and are by no means limited to single alveoli. The alveolar walls are greatly thickened, partly by contraction, but partly also by a new formation of connective tissue and infiltration with wandering cells. The epithelium forms a continuous layer of high cubical cells extending also over the connective-tissue strands in the lumen.

Thus it is evident that this process is one which has proceeded to a sort of healing with interstitial new growth, organization of the exudate and induration of these affected patches of the lung. The remaining lung tissue is normal. It is to be noted that there is no pleural exudate, and that the lung is dry and for the most part air-containing, and further that where bacteria are still found there is a thoroughly well resisted invasion with advanced barricade formation.

Case 81.—C. K. Onset on September 22, 1918, with deafness, coryza and headache. Entered hospital on September 27, with ear drums injected but not bulging, complaining of headache. There was a dusky cyanosis with fever of 100-103° F. Resonance impaired over both backs, with large moist râles. On October 5, bronchial breathing in left scapular region, many crepitant râles. Cyanosis became deeper and the patient passed into coma and died on October 11, 1918. Autopsy two hours after death. Sputum and mouse inoculation therefrom showed both gram-negative and gram-positive diplococci. The sputum contained many gram-negative bacilli.

Anatomical Diagnosis.—Bilateral disseminated organizing and interstitial bronchopneumonia.

Rectus muscles normal.

The *left pleura* is obliterated anteriorly by easily torn adhesions, but posteriorly there is about 300 c. c. of fluid. The posterior surface of the lung is covered with thick honeycomb-like fibrin which glues the lobes together and binds the lung to the diaphragm and to the pericardium.

The *right pleura* is entirely obliterated by delicate adhesions.

In the *left lung* (Fig. 19) the bronchial lymph glands, like those of the retrosternal region, are large, soft, greyish and moist. The lung is voluminous, but not heavy. The upper lobe externally is mottled with grey red patches, alternating with air-containing lobules. A similar condition ex-

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tends throughout the lower lobe and posteriorly both are flecked with small hæmorrhages and roughened with fibrin. On section the whole lung is studded minutely with firm, grey prominent nodules which are widely placed about the ends of the bronchioles. They measure only 1 or 2 mm. in diameter and are found in groups of three or four on the cut surface of each lobule.

The *right lung* (Fig. 18) is very large and everywhere appears to contain shot-like nodules in its substance. The edges of the lower lobe are air-containing, the rest is purplish grey.

On section the bronchi are deeply reddened with an opaque film over the surface of the mucosa. The lung substance is largely air-containing, but it is thickly studded with fine nodules which are about 1.5 to 2 mm. in diameter and usually grouped in twos and threes. They are greyish, fairly translucent and frequently surrounded by a zone of hæmorrhage.

Cultures from both lungs and from the trachea show the presence of Pfeiffer's influenza bacillus alone. Smears from the lung and sections show the same thing.

Microscopical Examination.—Sections from various parts of the lungs show practically the same conditions. The pleura is somewhat thickened and infiltrated with mononuclear cells and is roughened by old adhesions. The interlobular septa are not very conspicuous, but are thickened and dense and much infiltrated with plasma cells and other mononuclears. The lymphatics are scarcely to be seen and are not evidently thrombosed. The areas of consolidation are formed round the bronchioles, and in many cases in which they are very minute and scattered in otherwise normal lung they consist in a thickening of the bronchial wall with the involvement of only a few adjacent alveoli (Fig. 20).

The bronchioles usually possess an intact columnar lining epithelium, although some have lost it in places or entirely. The walls are very greatly thickened, but the thickening is due not to œdema or hæmorrhage, but to a new formation of connective tissue and a dense infiltration with mononuclear cells of which the majority are easily recognizable plasma cells. The adjacent alveolar walls are greatly thickened, both by new formation of connective tissue and infiltration with cells. The epithelium is sometimes entirely desquamated, sometimes well preserved or even greatly thickened and hyperplastic. It is, when present, often lifted up with the structureless basement membrane from the centrally placed capillaries of the wall by accumulations of mononuclear cells or leucocytes.

The bronchioles contain an exudate almost entirely made up of polymorphonoclear leucocytes which contain many influenza bacilli. These bacilli are not present in great clouds, but are enclosed in the leucocytes in threes and fours. Relatively few are free. No other organisms are to be seen. In the alveoli the exudate is also composed of polymorphonuclear leucocytes often mixed with a large fat-holding, desquamated epithelial cell. These large cells are actively phagocytic and are filled with the remains of other cells, usually leucocytes. As a rule no influenza bacilli are found in the alveoli, especially in those areas where the alveolar

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walls are much infiltrated and thickened. Such areas indeed often contain in the alveoli very few leucocytes, but masses of dense fibrin with mononuclear wandering cells. Organization of this exudate is well under way, but is by no means complete. It is quite absent in those areas in which the alveolar exudate is rich in leucocytes. It is to be noted that of the mononuclear cells infiltrating the septum, bronchial walls and alveolar walls, practically all are lymphoid and plasma cells with some larger elements with slightly basophilic cytoplasm. There are no mast cells, nor are there any megalocaryocytes in the capillaries. There is no evidence of thrombosis of capillaries, although some larger veins occasionally show mural or obstructive thrombi.

More active processes are also to be observed in that there are abscess-like cavities in the consolidated tissue filled with leucocytes, but without any definite wall other than the adjacent alveoli with their fibrinous contents. The leucocytes contain the influenza bacilli. These abscesses are so minute as to be overlooked in the naked eye inspection. There are also patches of lung tissue quite away from the indurated areas or sometimes contiguous with them in which the alveolar walls have undergone no infiltration or thickening, but in which the alveolar cavities are packed with leucocytes loaded with influenza bacilli. These are minute areas of fresh pneumonic consolidation in a lung which has elsewhere responded to the invasion by producing indurated patches about the infected bronchioles with much barricade formation and successful restriction of the bacilli.

Case 86.—M. F. F. Aged 30 years. Onset on September 22, 1918, with coryza, slight cough, no malaise or sore throat. Was admitted to the hospital September 24. There is no further note until October 6, when there were râles in the right lung with dullness, frequent and shallow breathing and slight delirium. On October 8 the delirium was more marked. The right lung flat behind with râles. Some râles over the left lung. On October 11 the patient became very dull and irrational, dyspnœa became very marked and death occurred on October 13. Temp. 103-99°. Pulse 100-160. Resp. 24-48. Autopsy one hour after death.

Anatomical Diagnosis.—Disseminated interstitial bronchopneumonia, bilateral. Subacute endocarditis.

The *rectus muscles* show an area of pallor in the lower portion with hæmorrhages in the substance of the muscles.

The *left pleura* contains 100 c. c. of opalescent fluid. The posterior diaphragmatic and mesial surfaces have lost their gloss, but the remainder is glistening.

The *right pleura* contains 50 c. c. of slightly turbid fluid. The surfaces are glued together almost everywhere by fresh fibrinous exudate.

The *left lung* (Fig. 21) is large and air-containing. The bronchus is filled with a thick yellow, purulent, mucus. The bronchial glands are large, firm and clear. The upper lobe is air-containing throughout, but studded with small shot-like nodules which can be felt everywhere. The lower lobe shows

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several bluish, elastic, shrunken patches, but is also filled everywhere with shot-like nodules. On section the cut surface of the upper lobe is uniformly studded with small nodules which are sometimes grouped in twos and threes. There are two areas of larger size in which these nodules are embedded in a clear, translucent, firm tissue, the cut surface of which is smooth. In the lower lobe there are similar areas of smooth, clear, translucent consolidation in which the bronchiole can be made out as the centre of denser nodules and the remainder of the lower lobe shows scattered nodules precisely similar to those in the upper lobe, but otherwise it is pale and air-containing.

The *right lung* is voluminous, pale, and for the most part air-containing. There are several firm patches in the posterior part of the upper lobe measuring about 2 cm. in diameter, and there are numerous small shot-like nodules scattered throughout the rest of the lobe. In the lower lobe there are three or four patches bluish grey in color, which on section appear as translucent areas studded with rather firm nodules. The remainder of the lobe presents many minute nodules of the same general character.

Heart.—The mitral valve is partly covered by large rounded vegetations which are fairly firm, but can be crushed rather readily.

The *trachea* contains a greenish yellow purulent mucus. Its mucosa is slightly reddened. The *larynx* is normal in appearance.

Cultures and smears from the trachea, large and small bronchi, from the substance of the right and left lungs, give the *B. influenzæ* alone.

Microscopical Examination.—Sections from various parts of both lungs show practically the same things. The pleura is thickened over the elastic membrane (which remains undisturbed) by a layer of granulation tissue upon which lies a thin film of dense fibrin. The interlobular septa are not especially conspicuous, but they are dense and thickened and infiltrated with plasma cells and other wandering mononuclears. The bronchi and bronchioles retain their lining layer of columnar epithelium intact and are filled with an exudate of polymorphonuclear leucocytes without much fluid or any fibrin. In this exudate influenza bacilli are fairly numerous and unmixed with other organisms. The walls of the bronchi are greatly thickened, chiefly by a new growth of connective tissue which lies both directly beneath the epithelium and outside the muscle. This is true of the small bronchioles and the thickening extends to the ductules and alveolar walls. It appears that the thickening of the walls of the alveoli is associated with their contraction, for the elastic tissue takes a tortuous course through them, although it is stretched straight in the walls of all the air-containing alveoli near by. About the bronchi there are thus formed areas in which all the framework of the lung tissue is greatly thickened so that in such areas it is dense and firm (Fig. 22). These are the nodules palpable and visible in the gross as dense greyish yellow masses. Between them the lung substance is normal with air-containing alveoli with thin walls. The consolidated areas are, however, not all alike, for in some the walls of the bronchioli and of the neighboring alveoli are densely infiltrated with leucocytes and the alveoli, like the bronchioli, are

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filled with similar polymorphonuclear leucocytes. There are some influenza bacilli in the exudate of the alveoli, but fewer than in that of the bronchi. In these bronchial and alveolar walls there are also many plasma cells, but they are overshadowed by the leucocytes. In other areas the surrounding alveoli are filled with dense fibrin masses which contract away from the walls, and, while containing many mononuclear cells, are partly organized by new connective tissue and are covered with newly formed epithelium. In the center of such an area is the bronchiole still filled with its purulent exudate. In other areas there is a less conspicuous exudate which is practically completely organized. In all cases the walls of the bronchi, of the blood-vessels and of the alveoli themselves are infiltrated with mononuclear cells, most of which have the character of plasma cells.

The thick alveolar walls are made more striking by the changed appearance of the lining epithelium, which is usually well preserved. The cells have become cubical or columnar and form a continuous thick lining. In some cases the epithelium has proliferated into a solid mass which has almost, or even completely, filled the alveolus. Such tumor-like growths of epithelium are very striking, but are rare in this lung and involve only two or three alveoli. In no instance is there any dilatation of the thick-walled bronchi.

Case 87.—J. J. S. Admitted to the hospital September 24, 1918. There is no note until September 28, when there were found dullness, râles and tubular breathing at the right base. By October 8 the right lower lobe was evidently densely consolidated, and on October 11 this was found to have involved the middle lobe. The heart then appeared slightly enlarged and there was an apical systolic murmur. On the afternoon of October 11 there began hemianopsia with anæsthesia of the left side of the head, face and chest and paresis of the left arm. The temperature ranged from 98-104°; pulse 84-120; respirations 24-48. Leucocytes, 17,600 with 95% of polymorphonuclears. The patient died, October 12, about three weeks after the onset of the illness. Autopsy four hours after death.

Anatomical Diagnosis.—Bilateral interstitial bronchopneumonia with abscess formation; multilocular encapsulated empyema; adhesive pericarditis; subacute endocarditis; fibrous myocarditis; infarcts of spleen and kidney; acute splenic tumor; bilateral abscesses of rectus abdominis muscles; chronic fibrous orchitis.

The *recti abdominales* show a hæmorrhagic effusion beneath the peritoneum. On incision it is found that there is on each side, in a symmetrical position, a large elliptical or lenticular abscess filled with thick yellow pus and surrounded by a dense wall with a hæmorrhagic zone. The adjacent muscle substance is pale.

The *left pleura* contains 500 c. c. of clear fluid. The surfaces are smooth and glistening.

Right Pleura.—On lifting the sternum a large pocket between the mesial surface of the right lung and the pericardial sac was opened into and found to contain thick greenish yellow pus. The right pleura is in large

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part obliterated by old adhesions, but there are several isolated empyema cavities—two on the outer surface of the lung each containing 80 c. c. of thick greenish pus, that between the lung and the pericardial sac which contains about 150 c. c. of similar pus and a small one between the diaphragm and the lung.

Heart.—Both aortic and mitral valves are thickened and scarred and on the ventricular surface of the mitral there are fresh vegetations which are continuous with an abscess-like infiltration in the myocardium.

Left Lung.—The upper lobe is in general air-containing, but on section presents scattered indefinite areas of consolidation. The lower lobe is discolored superficially by hæmorrhagic blotches. Nodular areas of consolidation can be felt in its substance, and on section these appear as red patches which are not very firm and show no definite plugs of exudate.

Right Lung.—The surface of the lower lobe, where it forms the wall of the empyema cavity, is ragged and yellowish green. There is an abscess cavity in its substance, partly filled with a shreddy yellowish green necrotic tissue through which air can be blown from the bronchus. The bronchus opens widely into this cavity. There are extensive areas of consolidation in the upper and lower lobes, especially in the posterior parts, which are greenish red with numerous nodular areas which are more opaque greenish grey.

Cultures showed in the trachea Pfeiffer's bacillus as the predominant organism, but there were also pneumococci, Friedländer's bacillus and Staphylococcus albus. The bronchi show Pfeiffer's bacillus, as do the minute bronchioles, but cultures from the lungs gave a Pneumococcus IV, staphylococcus albus and Friedländer's bacillus. The rectus muscle and the pericardium showed in culture Pneumococcus IV. Mice inoculated from the lungs gave in each case a mixture of Pneumococcus IV and Pfeiffer's bacillus. It is evident that the long duration of the case with its empyema and abscess formation is correlated with this great mixture of bacteria.

Microscopical Examination.—The microscopical examination of these lungs shows that the areas of consolidation in the left are small patches which represent a somewhat earlier stage, but one otherwise identical with those in the right. The sections through various parts of the right lung show a thick layer of frayed fibrous tissue in the position of the pleura; where the section enters one of the empyema cavities there is a layer of granulation tissue. One passes through the abscess and shows ragged shreds of partly necrotic lung tissue hanging in a mass of leucocytes. Among these leucocytes can be found a few pneumococci, but no influenza bacilli. Elsewhere the thickened pleura is continuous with dense, rather wide interlobular septa which are really fibrous and show no conspicuous lymphatics. Such lymphatics as were seen were plugged with connective tissue replacing a thrombus. There is no marked infiltration of cells in the fibrous septa. The bronchi have an intact lining of columnar epithelium. They are not dilated, nor are their walls very conspicuous from interstitial new growth of tissue, or infiltration with mononuclears. All

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the bronchi and bronchioles contain an exudate of polymorphonuclear leucocytes, sometimes mingled with much blood. In some of the smaller bronchioles there are strands of connective tissue. The ductuli alveolares and some of the immediately surrounding alveoli are often widely distended with leucocytes. Swarms of influenza bacilli are found in this exudate, although they are not seen in the more distant alveoli, nor in the large abscess. Rather numerous pneumococci are also present, but no other organisms can be distinguished.

The lung substance in the consolidated areas is partly collapsed, the alveoli have very thick walls and are filled with an exudate which is largely composed of red corpuscles, desquamated epithelial cells and fibrin. In many if not most places the mass of fibrin is beginning to be organized and is partly or completely covered by new epithelium. No bacteria and few leucocytes are to be found in these alveoli. The large fat-laden phagocytic cells are surely epithelial cells, as they can often be traced into continuity with those in the walls. Mitotic figures are found in these cells.

The alveolar walls are hard to outline because they are thickened and brought almost together and because the epithelium is in most cases desquamated or has extended over those strands of connective tissue which are replacing the fibrin. They are infiltrated with plasma cells, especially where they adjoin a bronchus or vessel or interlobular septum. These are typical plasma cells and no other mononuclear forms appear. Most of the tissue of the framework of the lung is visibly infiltrated with these cells, which scarcely act as phagocytes.

In the neighborhood of some bronchioles and ductuli alveolares, an extensive new formation of epithelium has occurred so that the columnar epithelium of the bronchioles is continued into solid masses which are evidently composed of new cells and which fill the alveoli. These strands and masses of epithelium stretch into neighboring alveoli so as to resemble a cancerous growth.

This is a condition described by others in chronic forms of pneumonia and only meagrely represented in this series.

Case 88.—E. E. H. Onset on September 29, 1918, with cough and fever. The patient was admitted to the hospital October 3, with cough, pain in the left chest and general soreness. On October 5 there was dullness over the left base with many râles and bronchial breathing on both sides. On October 8 a friction rub was heard in the left anterior axillary region. On October 9 to 13 delirium, cyanosis and labored breathing. Temp. 102-99°. Pulse 97-140. Resp. 30-40. Death October 13. Autopsy four hours after death.

Anatomical Diagnosis.—Interstitial bronchopneumonia; fibrinopurulent pleuritis, left; hæmorrhagic necrosis of myocardium, left ventricle; rupture of rectus abdominis with hæmorrhage.

The *rectus muscles* both show hæmorrhage and rupture, but this is not very extensive.

The *left pleura* contains 1500 c. c. of cloudy lemon-yellow fluid. The surfaces are covered with fibrin which, in the posterior part of the cavity,

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becomes a great, shaggy, thick mass, the meshes of which are filled with fluid.

The *right pleura* is partly obliterated by old adhesions which contain in their meshes about 80 c. c. of turbid yellow fluid.

The *left lung* is almost entirely air-containing, but is studded throughout with firm greyish nodules. In the lower part of the upper lobe there is an area about 3 cm. in diameter which is firm and airless; in the posterior part of the lower lobe there is a similar area. Both of these are studded with smaller greenish nodules.

The *right lung* is roughened over its whole surface. In general it is air-containing, but as seen on section shows numerous small greyish areas which are related to the bronchioles. There are also some small patches of grey, rough, consolidated tissue.

Heart.—The valves are delicate and the endocardium is smooth. The myocardium is opaque and greyish red and in the wall of the left ventricle, near its base, there is a red opaque patch about 1 cm. in diameter.

Cultures and smears from the trachea and the bronchi showed the bacillus influenzæ. Those from the left lung and pleura showed pneumococci, which were also found in the heart blood and the pericardium.

Microscopical Examination.—The changes in the right and left lungs are alike except for the pleural exudate, which upon the left is composed of a loose network of fibrin with relatively little invasion of connective tissue, but loaded with leucocytes. Numerous pneumococci are found among these cells, but not within the lung. The pleural membrane itself is greatly thickened by new granulation tissue. The elastic membrane is lifted up by this, but the blood vessels and fibroblasts penetrate it and form a layer on the outside. The interlobular septa are thickened and dense and composed of connective tissue in which there is very little infiltration of cells and no œdema. The bronchi and bronchioles contain an exudate composed of leucocytes, many of which enclose several influenza bacilli. No other bacteria are seen there nor in the substance of the lung. The epithelial lining is usually intact; the connective tissue of the wall is spread apart and greatly increased in amount. In most places it is densely infiltrated with mononuclear cells, some of which are lymphocytes, some characteristic plasma cells, while others are larger and more irregular mononuclear wandering cells. A few cells with basophilic granules occur there.

The blood-vessel walls are very little altered and there are no thrombi. The bronchioles are in many places surrounded by areas of altered tissue and, indeed, as observed by gross inspection, this alteration often becomes confluent so as to produce quite large firm patches. In all cases the walls of the ductuli alveolares and of the alveoli are greatly thickened, partly by actual new formation of connective tissue, partly by infiltration of mononuclear wandering cells. The epithelium of the alveoli is swollen and forms a thick layer of large plump cells, but in many of the alveoli it is almost entirely desquamated and floats there as large rounded phagocytic cells. In some places the epithelium is greatly proliferated so that it forms solid masses of fresh cells which stain deeply and almost fill the

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alveolar space. This is the proliferation which has been noted as even more conspicuous in other cases. The exudate within the alveoli is in some places rich in fibrin—indeed, it consists of a dense retracted mass of fibrin entangling a few cells and in many places entirely overgrown by a covering layer of new epithelial cells. Some groups of alveoli, on the other hand, are packed like the bronchioles with dense masses of polymorphonuclear leucocytes, many of which contain influenza bacilli, but no other organisms.

Nearly everywhere there is an active organizing process which leads to the rapid invasion of the fibrinous exudate within the alveoli and ductules by new connective-tissue cells. This differs in no way from the organization of an exudate in the lung in other cases and presents the same long ramifying strands of new tissue stretching from the bronchioles into the alveoli. It gives the density and translucence to the consolidated areas while the foci of leucocyte accumulation in the alveoli coincide with the greenish opaque spots in the grey tissue.

The lymphatics are not readily seen and are nowhere distended or thrombosed.

Case 89.—W. H. Aged 23 years. Onset on September 19, 1918, with chills and fever, and the patient was admitted on September 24. He became delirious on October 1, with râles through both lungs and dyspnœa. On October 7 there was dullness in both lower lobes. Temp. 102-99°. Pulse 75-130. Resp. 28-58. Died October 13. Autopsy five hours after death.

Anatomical Diagnosis.—Bilateral disseminated interstitial bronchopneumonia; old pleural adhesions; acute fibrinopurulent pericarditis.

Rectus Muscles.—The upper segment of both recti show marked pallor; the lower portions are normal. There is no rupture or hemorrhage in the muscle.

The *left pleura* is partly obliterated by old adhesions.

The *right pleura* is also largely obliterated by old adhesions.

The *left lung* is covered with tags of old adhesions. The posterior and lower part of the upper lobe is firm and nodular (Fig. 23). It is covered with hæmorrhages. On section, the upper part is air-containing, but the lower portion is purplish gray, firm, quite airless and smooth. The bronchi and blood vessels are conspicuous. The consolidated area is somewhat spongy, but the spongy structure seems filled with a translucent material which gives a smooth surface. There are also yellowish grey points of consolidation which have central lumina as though representing bronchioles. The lower lobe is filled with firm nodules which are easily cut. In its upper portion there is an area of consolidation which on section shows many small opaque yellow nodules closely set in a purple background. The bronchial glands are large, grey and firm.

The *right lung* is densely adherent over its whole surface and very voluminous. The bronchial glands are firm, large and greyish red. The upper lobe is generally air-containing, but shows one or two consolidated lobules in the extreme posterior part which on section are dark red in

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color, are not very firm but œdematous. The middle lobe is air-containing throughout. The lower lobe contains several nodules of firm consistency. On section the cut surface is sprinkled with small hæmorrhagic areas with grey central opacity. These measure not more than 3 or 4 mm. in diameter.

Heart.—The pericardium contains about 300 c. c. of turbid greenish fluid. The whole pericardial surface is rough and granular looking with hemorrhages and a rather thick layer of fibrin which hangs from both membranes in long strands about 1 mm. in thickness. These give the heart an extraordinarily hairy appearance.

Cultures from the blood, pleura and lungs failed to grow, but a culture from the pericardium gave a hæmolytic streptococcus. Sections and smears from the bronchi and lung showed Pfeiffer's bacillus.

Microscopical Notes.—The right lung is more extensively altered than the left in that the pleura is greatly thickened, and broad, dense, interlobular septa run through the tissue. In principle, however, the changes are alike. The interlobular septa are widened not by œdema, but by newly formed connective tissue. The lymphatics are very inconspicuous, but sometimes contain fresh fibrinous coagula. The bronchi and bronchioles are profoundly altered. They are in most cases lined with an intact layer of epithelium which is permeated by leucocytes. They contain a purulent exudate which is loaded with influenza bacilli in swarms, but contains no other organisms. Many of the smaller bronchioles have lost part of their epithelium, which is crumpled together in the middle, and are occupied partly by a fibrinous coagulum, partly by vascular granulation tissue which springs up everywhere from the wall. Such columns of newly formed connective tissue are numerous and extend, obliterating the lumen, from the bronchiole down into the ductulus and into the air cells. The walls of the bronchi and bronchioles are greatly thickened by new connective tissue and densely infiltrated with mononuclear cells, lymphocytes, plasma cells and larger mononuclears.

The blood vessels are less affected, but many of the more terminal branches, arteries as well as veins, are blocked with peculiar thrombi which are almost entirely made up of leucocytes. No bacteria can be found in these thrombi and only a delicate network of fibrin.

The alveolar walls are thickened and in many cases also infiltrated with mononuclear cells. They contain an exudate which is very hæmorrhagic, but which in most cases is largely replaced by the organizing connective tissue. Where the exudate appears to be fresh, it is composed chiefly of red corpuscles and a few lymphoid cells, or of pure blood.

Two small bronchioles were found to contain radially arranged masses of some form of sporotrichum, but search elsewhere failed to reveal any more of it. It seems probable that it had little or nothing to do with the development of the widespread lesion. A hæmolytic streptococcus was obtained in culture from the lungs, pleura and pericardium, but since none could be found in sections of the lung, in the presence of myriads of influenza bacilli, its part also seems negligible.

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CASE 91.—C. F. W. Taken sick six weeks ago with chills, coryza and general malaise. Was in bed four weeks, got up for several days and then went back to bed. Admitted to hospital October 5, 1918, with distant breath sounds, slight dullness over the backs and evidences of the presence of fluid in the chest. Moist râles and bronchovesicular breathing over both lower lobes. There was albuminuria. Temperature 103-100°. Died October 14, 1918. Autopsy one hour after death.

Anatomical Diagnosis.—Lobular pneumonia (right) with abscess formation and empyema.

The *left pleura* is partly obliterated by adhesions, but the posterior part of the cavity contains about 130 c. c. of greenish purulent fluid.

The *right pleura* is obliterated anteriorly by adhesions, although there is a pocket of pus between the fifth and sixth ribs partly overlying the pericardium. There are several smaller cavities formed among the adhesions over the surface of the lung and filled with pus. While these are circumscribed and flattened, the one overlying the pericardium extends backward to communicate with the main pleural cavity which forms a sac lined with yellowish granulation tissue and a fibrinopurulent exudate, consisting of about a litre of thick greenish pus.

The *left lung* is quite collapsed, but can be insufflated and is then found to be air-containing throughout.

In the *right lung* the upper lobe is collapsed, soft and pasty, but shows no areas of consolidation. The lower lobe is bulky and fairly firm, but fluctuant in its posterior part. On section it is found to contain many ramifying abscess cavities into which hang shreds of necrotic tissue. The largest of these in the posterior part of the lung measures 6 cm. in diameter and is filled with necrotic debris. The surrounding lung tissue is firm, very yellow and presents a rather rough cut surface.

No cultures were made.

Microscopical Examination.—Sections through the right lung show that the pleura is greatly thickened by a new growth of granulation tissue through which abundant vessels spring up into the overlying fibrinous exudate. Pneumococci are found in this exudate.

The interlobular septa are broad and dense and moderately infiltrated with mononuclear wandering cells. The lymphatics are frequently thrombosed and, in some instances, enormously distended into abscess-like cavities filled with a purulent exudate which is bordered by a layer of large vacuolated mononuclear cells.

The substance of the lung in general is indurated by the thickening of all the skeletal tissues; the walls of the bronchi and blood vessels are similarly thickened and infiltrated. The bronchi are not dilated, their epithelium is usually intact and they contain a purulent exudate rich in pneumococci and containing some influenza bacilli.

Large abscesses are scattered throughout the section. In some of these the contour of the necrotic lung substance can be traced for a great distance. In others the alveolar walls are destroyed and the cavity contains only a fluid purulent exudate. The surrounding tissue presents marked

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alteration, but scarcely of the type of an ordinary pneumonia. Instead the alveolar walls are everywhere thickened and somewhat infiltrated with mononuclear cells. The alveolar epithelium is prominent and deeply stained. The cells seem almost to hang into the lumen on stalks, and the wall presents, therefore, a scalloped appearance. The cavities of the alveoli are practically filled with clumps of very large cells with shrunken wrinkled nuclei and foamy vacuolated protoplasm. It is impossible to say certainly whether these are desquamated epithelial cells or not, but since their nuclei are unlike those of the definite epithelial lining cells in that they have not a conspicuously stained nucleolus, it seems possible that they may be swollen mononuclear phagocytes, especially since there are many of these cells mingled with them. The suggestion is further supported by the fact that the larger vacuolated cells are sometimes found in the substance of the alveolar or bronchial walls.

In many alveoli this cellular exudate is being invaded by new connective tissue and blood vessels, and overgrown by new alveolar epithelium. This organization, which occurs despite the fact that there is relatively little fibrin in the alveoli, leads to the formation of long strands which extend far through the tissue.

These cases have been grouped together because in them the influenza bacillus of Pfeiffer was the predominant and in several cases the only organism present. They agree very closely in the character of the changes in the lungs and differ from those in the preceding group chiefly in the absence of hæmorrhage and in the induration of the framework of the lung and the organization of the exudate. It seems possible that these differences may be accounted for by the fact that in these the illness had an average duration of nineteen days instead of thirteen as in the preceding group.

In cases 81 and 86, the influenza bacillus was present in pure culture; in cases 80, 88 and 89 it was practically the only organism present, but in cases 87 and 91 there were also many other bacteria with corresponding complications in the anatomical alterations in the form of abscesses, empyema, etc.

In those cases in which there was no obvious complication produced by other bacteria, we may expect to find the characteristic lesions produced by the influenza bacillus and this is particularly true of cases 81 and 86, but almost equally so of cases 80, 88, and 89.

There is no great amount of pleural exudate and indeed such as was present may be organized into adhesions which obliterate the pleural cavity. The lung is pale and dry and its cut surface is roughened by numerous projecting nodules which are grey or yellowish grey, translucent, and smoothly cut through with the knife. Each is seen to

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surround a central bronchiole which contains a minute droplet of yellow pus. Sometimes these nodules are confluent and form fairly large areas of grey, elastic, rather translucent tissue with foci of yellow opacity where the bronchioles present themselves on the cut surface. The larger bronchi are filled with thick yellow, sticky pus, which contains the influenza bacilli. The lung tissue between the firm nodules is air-containing.

Microscopically, there is infiltration of all the framework of the lung with wandering cells and much new formation of connective tissue so that the pleura, the interlobular septa, the bronchial and vessel walls, and even the alveolar walls in the indurated areas, are thickened and rendered dense by the addition of new cells and fibres. The lymphatics in these structures are not dilated nor do they contain bacteria—instead, they are often thrombosed or obliterated by the organization of such thrombi.

The bronchioles contain a purulent exudate with many influenza bacilli enclosed in the phagocytic leucocytes. Their epithelium is usually intact or interrupted in places from which there spring up columns of newly formed connective tissue which extend far into the corresponding alveoli. Their walls are densely infiltrated with mononuclear cells and often, also, with polymorphonuclear leucocytes. The alveoli contain an exudate composed of polymorphonuclear leucocytes with desquamated epithelial cells, fibrin and relatively few mononuclear or red corpuscles. The alveolar epithelium may be partly desquamated or it may have taken part in the organization of the intra-alveolar exudate and spread over the newly formed connective tissue in the lumen. In other cases, great hyperplasia of the epithelium occurs and the alveolus becomes almost filled by a mass of its new cells. The alveolar walls are infiltrated with leucocytes, less often with mononuclear wandering cells, and their thickness is increased by this as well as by the occasional new formation of connective tissue in their substance. All this applies to the peribronchial nodular areas of induration. The remaining air-containing lung substance is usually quite normal in appearance.

This lesion shows some points of resemblance to that described as interstitial bronchopneumonia following measles and said to be caused by the universally present streptococcus hæmolyticus. It is the more important that they should be compared, inasmuch as the influenza bacillus was found associated with the streptococcus in about one-

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third of those cases and it might be thought that it was responsible there also for the interstitial induration and organization of the exudate. It is, of course, a possibility and we decided that in one or two of those cases in which the influenza bacillus was the predominant organism (Case 37 of that series) it was almost surely responsible for the changes. There were, however, many cases, and those the most typical instances of the interstitial bronchopneumonia, in which, while streptococci were present in great numbers, no influenza bacilli could be demonstrated in cultures, smears, or in sections.

I have concluded, therefore, that both of these organisms are capable under proper conditions of producing an interstitial bronchopneumonia and have been able to recognize very considerable differences between these two forms. That produced by the hæmolytic streptococcus is characterized by the outpouring of a great pleural exudate loaded with streptococci which is due to the rapid transportation of the streptococci through the greatly dilated lymphatics of the lung to the pleural surface. The lung is consequently compressed and rendered atelectatic by the pleural exudate but it remains moist, bluish, and is studded throughout with nodules of firm consistency and of varying size. These are peribronchial and sometimes constitute mantle-like thickening of the bronchial wall, oftener clustered nodules about the terminal bronchioles. They are grey or yellowish grey, but conspicuously surrounded by hæmorrhage and œdema—indeed, the outer zones of such nodules are deeply hæmorrhagic. Polymorphonuclear leucocytes are found with the streptococci in the bronchioles but both are limited to that position and do not fill the alveoli. The alveoli, on the contrary, contain dense plugs of fibrin, mononuclear wandering cells, and blood. The alveolar walls are infiltrated like the bronchial walls with mononuclear cells and not with leucocytes.

Thus the influenzal interstitial bronchopneumonia differs from this in the pallor and dryness of the lung, the obliteration or inaction of the lymphatics which contain no bacteria, the absence of an intense infection of the pleura with outpouring of abundant pleural exudate, and further, in the fact that the alveolar as well as the bronchial exudate is usually composed of polymorphonuclear leucocytes, and that these invade the walls of the alveoli. It is true that in what we have described as a rather more acute form of pulmonary lesion caused by the influenza bacillus hæmorrhage is predominant, but this disappears when the organization of the exudate is well under way.

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Organization of the exudate is much more prompt and complete than in any of the cases of the streptococcal pneumonia, and the consequent induration of the peribronchial areas is much denser and due to the actual new formation of tissue rather than to infiltration with mononuclear cells.

Although it is not easy to describe in a convincing way the differences between them, there is such an extraordinary divergence between the gross and microscopical appearances of the lungs in the two conditions that there is really no difficulty in distinguishing them. In one we have a purple blue collapsed lung floating in an enormous pleural exudate with peribronchial nodules of grey, fairly firm, tissue composed of alveoli infiltrated and filled with fibrinous plugs embedded in hæmorrhage and œdema; in the other, a pale, dry, air-containing lung with no pleural exudate, and studded with firm, smooth, grey translucent nodules, peribronchial also but composed of alveoli with their walls infiltrated with leucocytes and filled with leucocytes and strands of tissue and not surrounded by hæmorrhage or œdema.

The upper respiratory passages were studied in these cases also and, while infection of their mucosæ was recognized in all the cases, the anatomical changes produced were rather slight. The frontal, ethmoid and sphenoid sinuses and the antrum of Highmore were investigated in a number of cases and it was usually found that the organism predominant in the lung was there also, although it was quite often the case that several other organisms were associated with it. Staphylococci were often found there, although perhaps not present in the lung. Thus, in cases 211, 214, 83 and 85 the sinuses contained a staphylococcus and the influenza bacillus. Cases 221 and 222 showed a pneumococcus in these sinuses. They were usually found to contain a purulent exudate.

The tonsils were but little affected and we thought that they played no important part in the inception or in the course of the disease. The pharynx was reddened and sore, especially in the cases in which the hæmolytic streptococcus was found. Moderate inflammatory reddening of the larynx was frequent in all the intense pneumonias but deep lesions with loss of substance and the disabling of the vocal cords were not observed. This was in sharp contrast with the great frequency of severe ulcerative laryngitis in the epidemic of streptococcal pneumonia following measles. In only three of these cases (82 and per-

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haps 221 and 230) was there even superficial loss of substance; on the other hand, a few cases showed deep reddening of the mucosa of the trachea sometimes with a pseudomembranous exudate (211, 217, 6133), while in almost all the others the larynx and trachea showed relatively slight changes and in many they were recorded as normal. Partly on this account and partly because sections of the trachea, even when there is a pseudomembranous exudate, have shown no extensive filling of the lymphatics with bacteria, I still incline to the view that the bacteria which reach the lung do so by way of the bronchial lumen.

General Summary

The study of these cases has been made with a view of determining, if possible, the nature of the infective agents which produced the disease and with the purpose of correlating, if possible, the anatomical changes in the tissues with the several ætiological factors.

No direct information has been gained as to the nature of the infective agent which with such great rapidity spreads throughout a community and causes the epidemic disease influenza, which is especially characterized by the remarkable speed with which it runs through the whole susceptible population. The diagnosis indeed is largely supported by the fact that the somewhat nondescript symptoms have appeared in the course of an epidemic of this sort, and we should have been cautious in admitting to this series any case in which death from pneumonia had followed an indefinite febrile affection with general aching and malaise, no matter how like the well recognized cases, if it had occurred at a time when there was no epidemic. Indeed, we may even feel somewhat cautious about accepting those cases which occurred in January and February of 1920, more than a year after the clearly outlined epidemic of 1918, although the outbreak had every appearance of being a recrudescence of the original epidemic disease and resembled it minutely.

It is our impression that epidemic influenza is a disease produced by some infective agent which differs from any of those which we have definitely recognized in that we cannot see it, nor stain it, nor grow it, nor infect animals with it. It has not even been artificially transferred to other human beings in spite of earnest efforts by several investigators. In most of these respects it bears a general resemblance to the infective agents which must be present in such exanthematic

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diseases as measles, scarlet fever, smallpox, etc., and, indeed, there is much to suggest a resemblance between the disease influenza and one or other of these exanthematic diseases. Bloomfield has observed a rash on the skin and in the mouth and pharynx and emphasizes his feeling that influenza is a form of exanthematic disease. One striking feature in which it further resembles some of these diseases is in the production of a great lowering of resistance to the invasion of bacteria and probably of other infectious agents. This appears to be associated with the leucopenia which is usually observed.

Whether any of the pathological alterations found in the lungs and elsewhere can be ascribed to the action of the influenza itself must remain rather uncertain, since no autopsy has been performed in which it was not found that the person had succumbed to a pneumonia in which bacteria were present in the tissues. The only lesion which is fairly common in these cases, and extremely uncommon in pneumonias produced by bacteria in ordinary times when there is no epidemic of influenza, is that which has been so frequently described above, the great dilatation of the ductuli alveolares with hyaline lining in the midst of a very fresh pneumonia. Goodpasture has suggested that this may be a true influenza effect and I am inclined to agree with him, although absolute proof is wanting.

Great confusion has been brought into the matter from the fact that Pfeiffer when he found a hæmoglobinophilic bacillus in the bronchi of many persons, long after the last great epidemic of influenza, named it the *B. influenzæ*. The name in itself seemed sufficient, when the recent epidemic began, to establish this organism in the minds of some as the actual ætiological factor in the disease. The bacillus is a very common and widespread one and is indeed an important pathogenic organism capable of causing various well-defined anatomical lesions and corresponding forms of disease. It need not be emphasized here that there are several distinguishable types, which are probably related to different conditions such as meningitis in children, etc. Furthermore, it was unfortunate that those who first encountered the disease in this country, with its attendant pneumonia, actually found the influenza bacillus as the predominant organism, with a type of pneumonia which has since been shown to be the characteristic result of its presence.

But study of the post-influenzal pneumonias in various camps and hospitals throughout the country ultimately convinced nearly every-

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one that this particular bacillus was by no means constantly associated with the disease and that there were many cases in which one or other type of pneumococcus was present in pure culture or in which the pneumonia was clearly due to the hæmolytic streptococcus. Those, especially, who themselves had opportunities of observing the disease in several widely separated places were readily convinced that, although the influenza was uniform and constant in every place, the type of bacterial infection producing the pneumonia differed with the locality and depended on local prevalence or upon the presence of carriers of some virulent organism and, therefore, upon the development of a local *epidemic* of streptococcus, staphylococcus, influenza bacillus, or other infection. That mixtures of various organisms commonly appeared was well recognized and it became quite clear that the bacterial invasion was essentially a secondary phenomenon, the result of the great lowering of the resistance of these individuals by the primary disease influenza which laid them open to infection of the intensest character with almost any organism which they happened to inhale.

This infection assumed the most destructive violence because the evident lowering of the resistance of the tissues left them to react merely like an inert culture medium in which bacteria could grow in unheard of quantities.

It is the especial aim of this paper to point out, as was done before in a brief summary, the typical reaction of such lungs to the invasion of special bacteria. While this has been belittled by several writers, the descriptions of the cases given above will show clearly enough that these typical forms of pneumonia are fairly readily recognizable. There is not the slightest difficulty in outlining precisely the type of change produced in the lungs by an intense infection with the hæmolytic streptococcus. Nor is there any difficulty in recognizing the very specific form of the pneumonic changes produced by the influenza bacillus, whether in its acuter or less acute form. The pneumonia produced by the staphylococcus we have hardly seen, but an epidemic has been described by Chickering in such a way that it could be readily recognized.

There remains the group caused by the pneumococcus and in these it must be said that the lesions produced have not the striking peculiarities of the other groups but are practically those which are all too familiar from their close correspondence with the effects of the invasion of pneumococci in the lungs of persons dying of pneumonia at times

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when there is no epidemic of influenza. Quantitatively and in the completeness or maturity of the lesion these pneumonias did not often reach the character of the ordinary lobar pneumonia. Death usually occurred when the consolidation was still patchy, and showed clearly its origin as a lobular affection, but except for the lesion which we have surmised to be an effect of the influenza itself there is no great difference between the character of the pulmonary changes in lobar pneumonia and in these cases. It is true that the inflammatory exudate is often, perhaps usually, much less homogeneous than that observed in lobar pneumonia, patches of dense consolidation being surrounded by zones of fresher exudate, hæmorrhage and œdema, but qualitatively there seems to be no fundamental difference between them. The enormous proliferation of the pneumococci, rapidly calling out an extreme œdema with hæmorrhage, gives these lungs a very moist, boggy character at first, but many of them in later stages showed extensive dry areas of uniform consolidation in which the alveoli and terminal bronchioles were packed with an exudate of leucocytes, fibrin and blood. The infiltration of the pleura with the overlying exudate, and of the interlobular septa and bronchi, is much less conspicuous than in the case of other infections and is of the character always familiar in pneumococcal infections.

Even in those cases which we have separated for the sake of emphasizing the lesion of the ductules, those instances in which the pneumococcus is the predominant or sole organism present show an exudate which is essentially of this character.

The others of that group, in which bacteria are few, are not numerous enough nor perhaps intensely enough infected to give a clear idea of what the type of lesion should be to correspond with the bacteria formed in them. One case (5706) contained scattered streptococci but so few that it certainly did not represent the type of streptococcal infection. So, too, with those which contained staphylococci and those in which only unidentified gram-negative cocci were found. Even the influenza bacilli which were found in two cases scarcely sufficed, it would appear, to produce any characteristic lesions. With these exceptions in which bacteria were present in such small numbers, all the cases fall naturally into their respective groups and maintain the characters peculiar to the effects of those bacteria.

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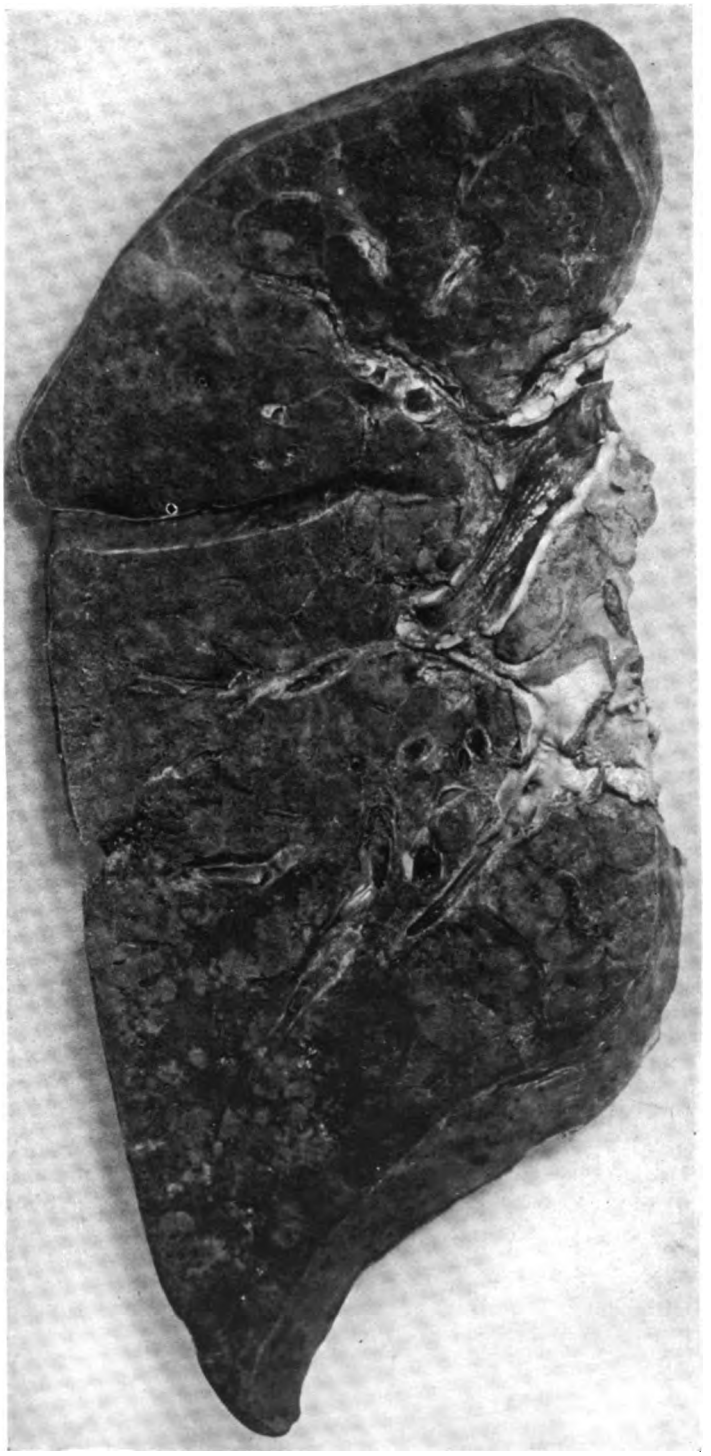

FIG. 1 (Case 218).—Confluent lobular pneumonia. *Pneumococcus IV.* In the lower lobe the consolidation is remarkably patchy. Pleural hæmorrhages over the base.

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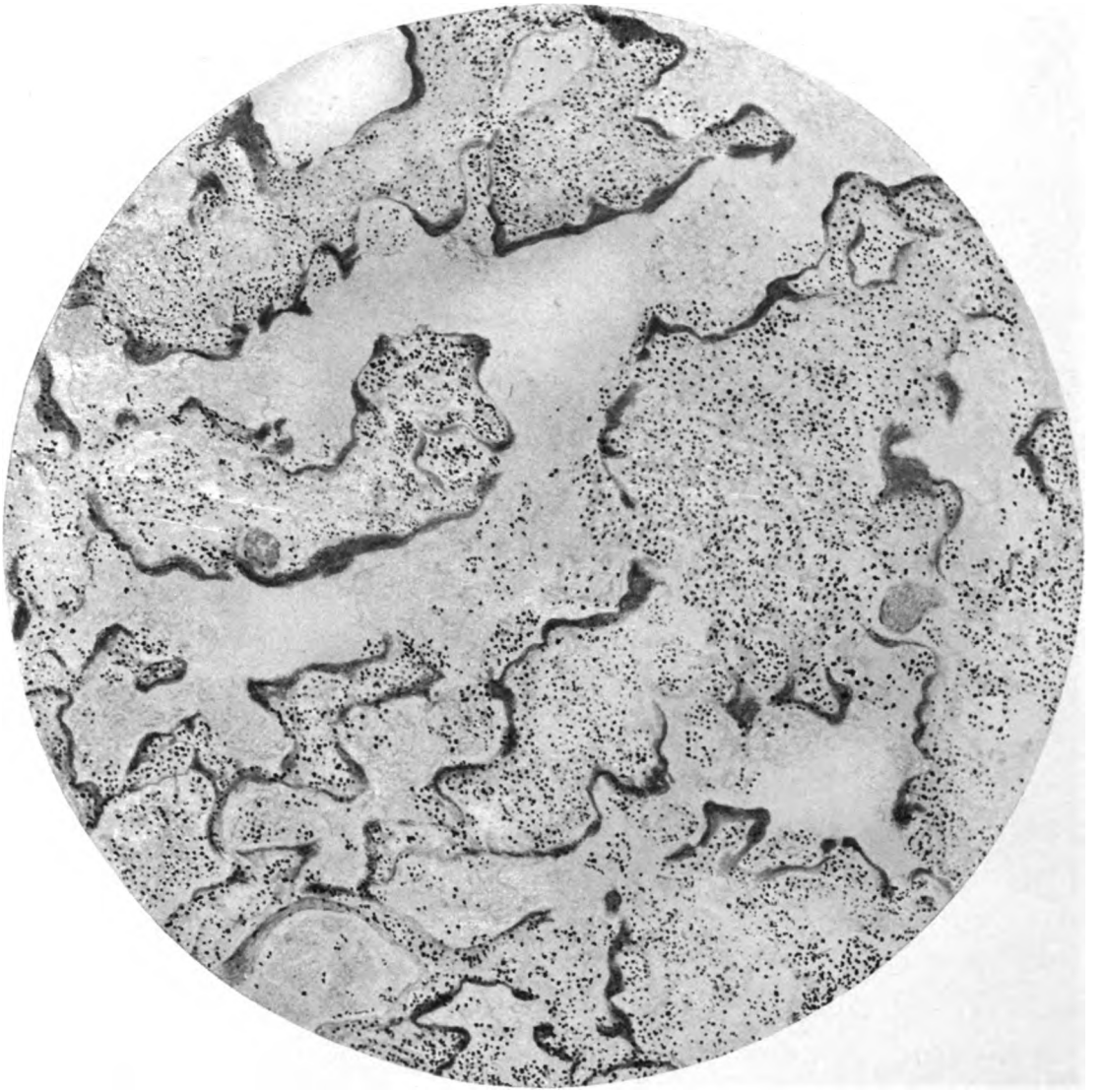

FIG. 2 (Case 223).—Fresh lobular pneumonia. *Pneumococcus IV*. The ductuli alveolares are dilated and lined with a hyaline layer. The exudate in the alveoli is very fresh.

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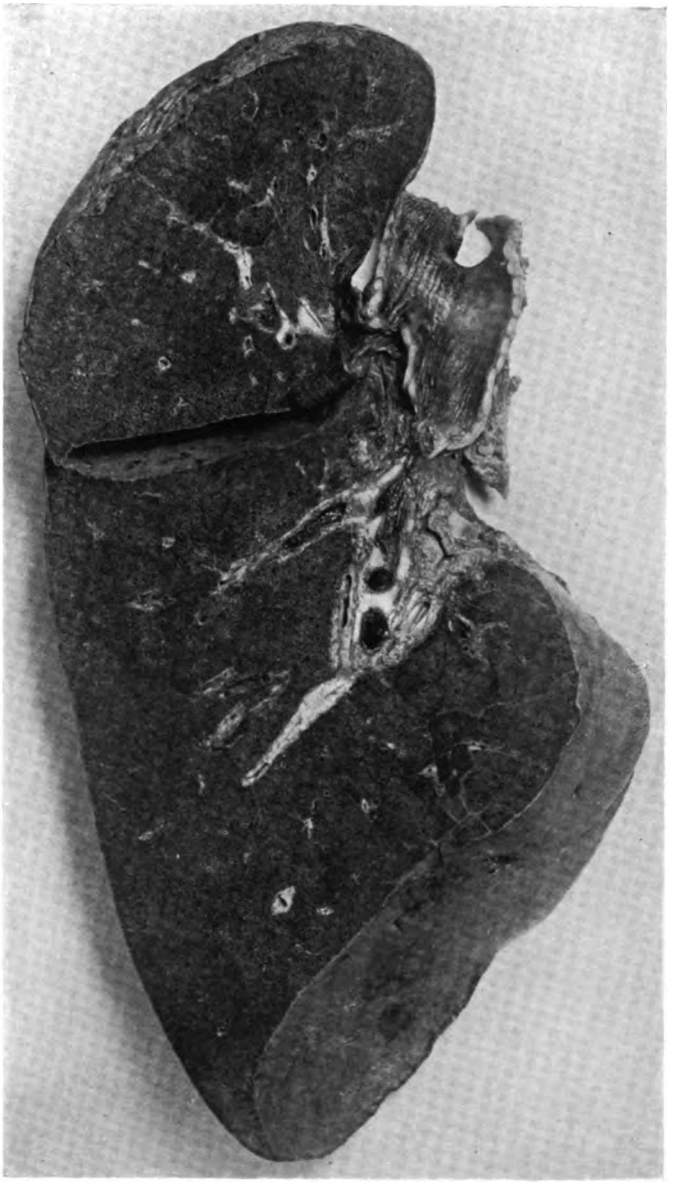

FIG. 3 (Case 224).—Right lung. Widespread fresh pneumonic consolidation with hæmorrhagic œdema. *Pneumococcus IV.*

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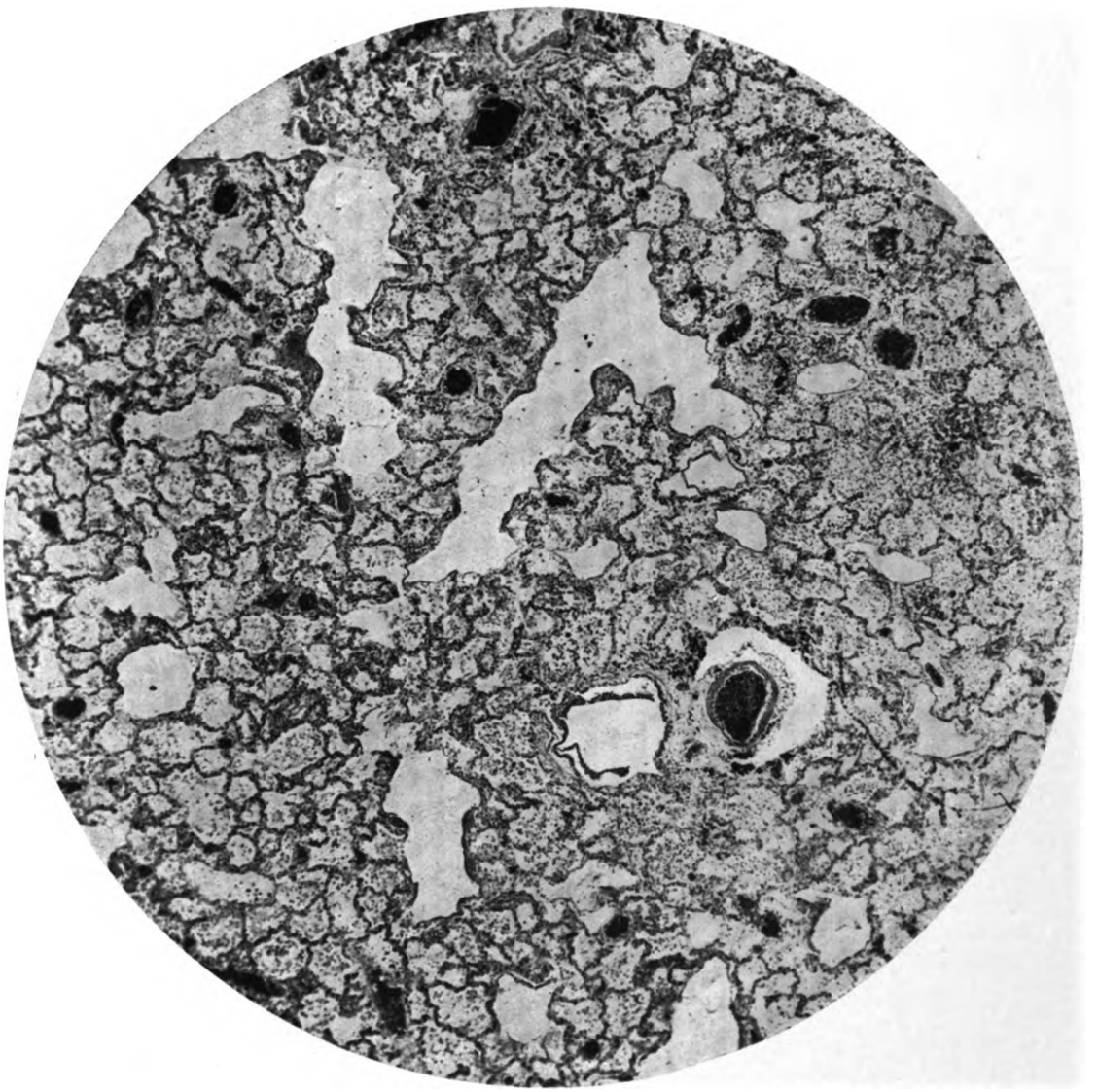

FIG. 4 (Case 224).—Fresh pneumonic consolidation with dilatation of ductuli.

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FIG. 5 (Case 224).—From the same case more highly magnified, showing the hyaline lining of the widened ductuli and abundant small mononuclear cells in the exudate. *Pneumococcus IV.*

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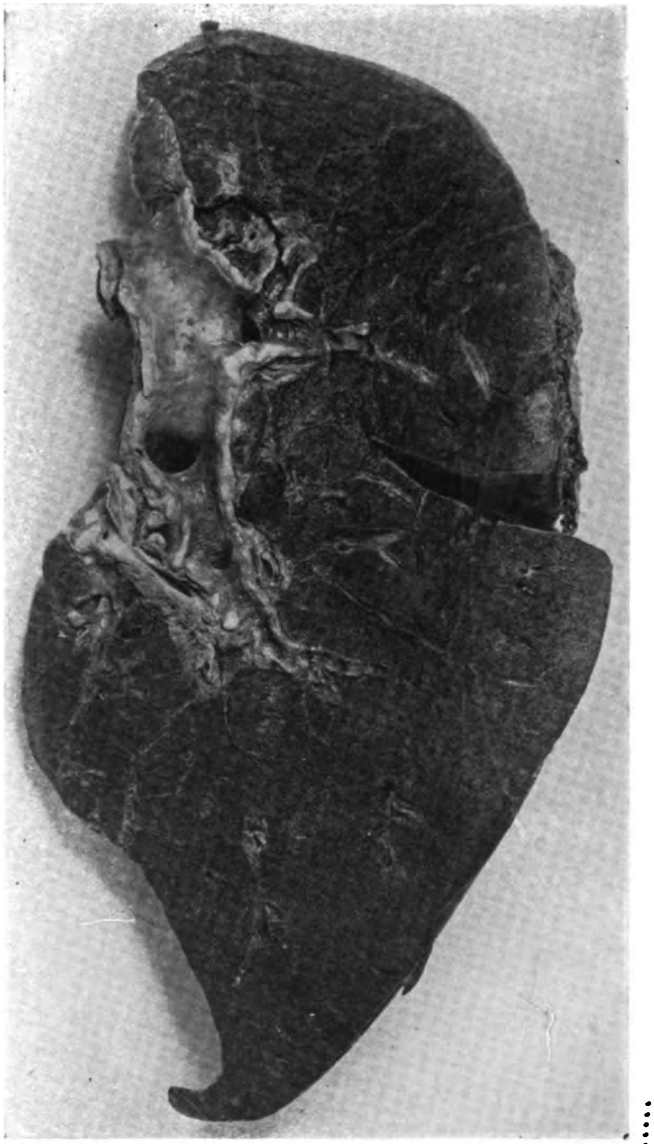

FIG. 6 (Case 82).—Right lung. Extremely fresh confluent lobular pneumonia. *Pneumococcus, M. catarrhalis, etc.*

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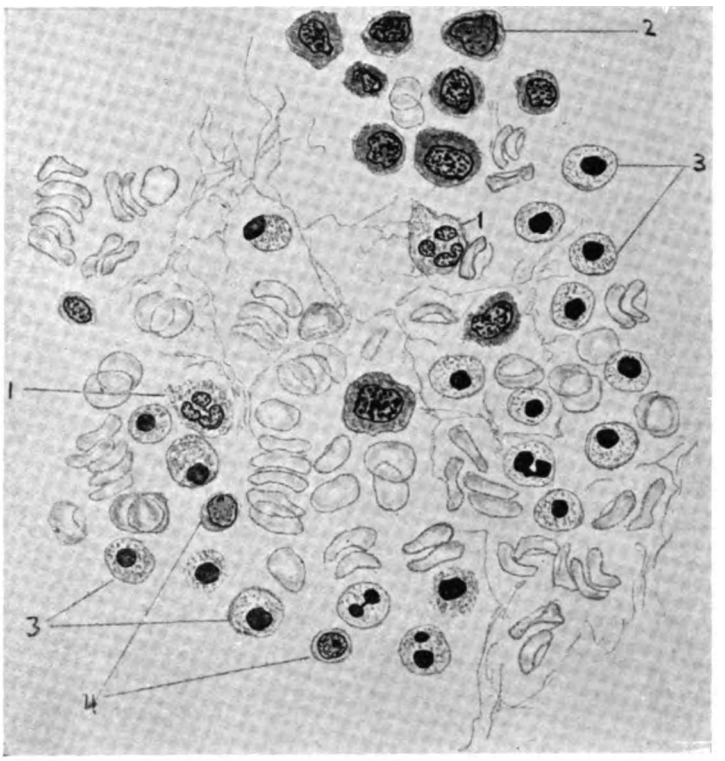

FIG. 7 (Case 82).—Part of the exudate from an alveolus, composed chiefly of red corpuscles with delicate strands of fibrin, but containing also (1) polymorphonuclear neutrophile leucocytes, (2) mononuclear wandering cells with rather basophilic cytoplasm, (3) the relatively small cells with deeply stained small round nucleus and neutrophile cytoplasmic granulations described in the text, and (4) lymphocytes.

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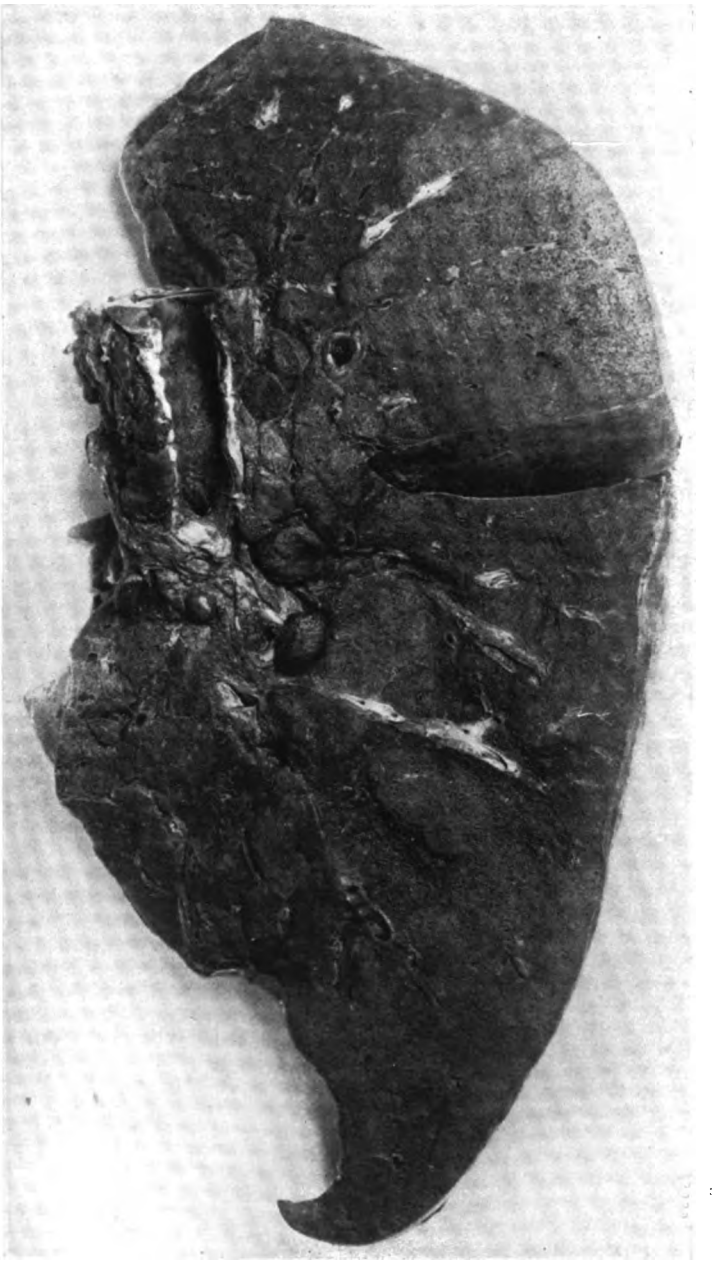

FIG. 8 (Case 211).—Right lung. Early confluent lobular pneumonia. *Staphylococcus and B. influenzæ.*

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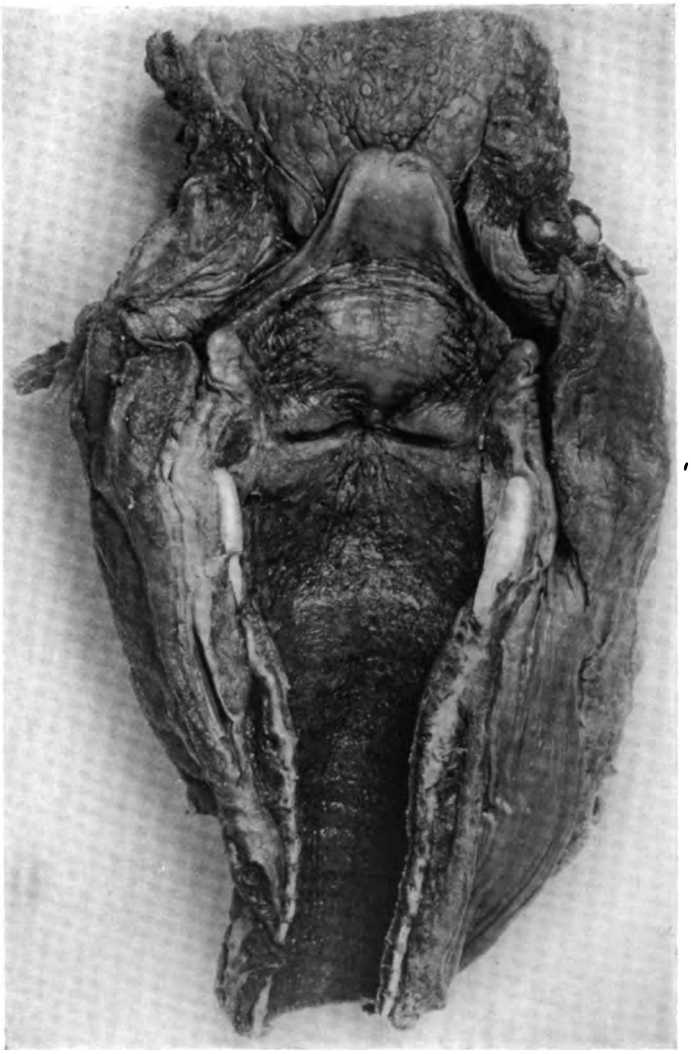

FIG. 9 (Case 211).—Pseudomembranous laryngitis and tracheitis.

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FIG. 10 (Case 83).—Left lung. Confluent lobular pneumonia. *Gram-negative coccus, possibly a meningococcus.*

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FIG. 11 (Case 216).—Right lung. Confluent lobular pneumonia. *Pneumococcus IV.*

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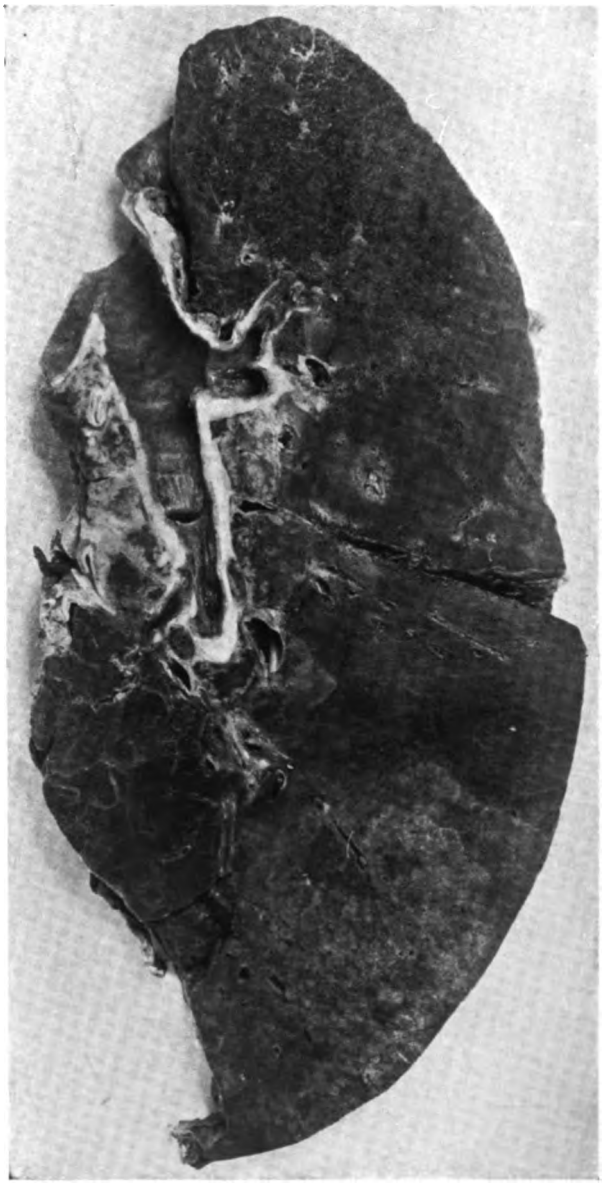

FIG. 12 (Case 227).—Right lung. Confluent lobular pneumonia. *Pneumococcus IV.*

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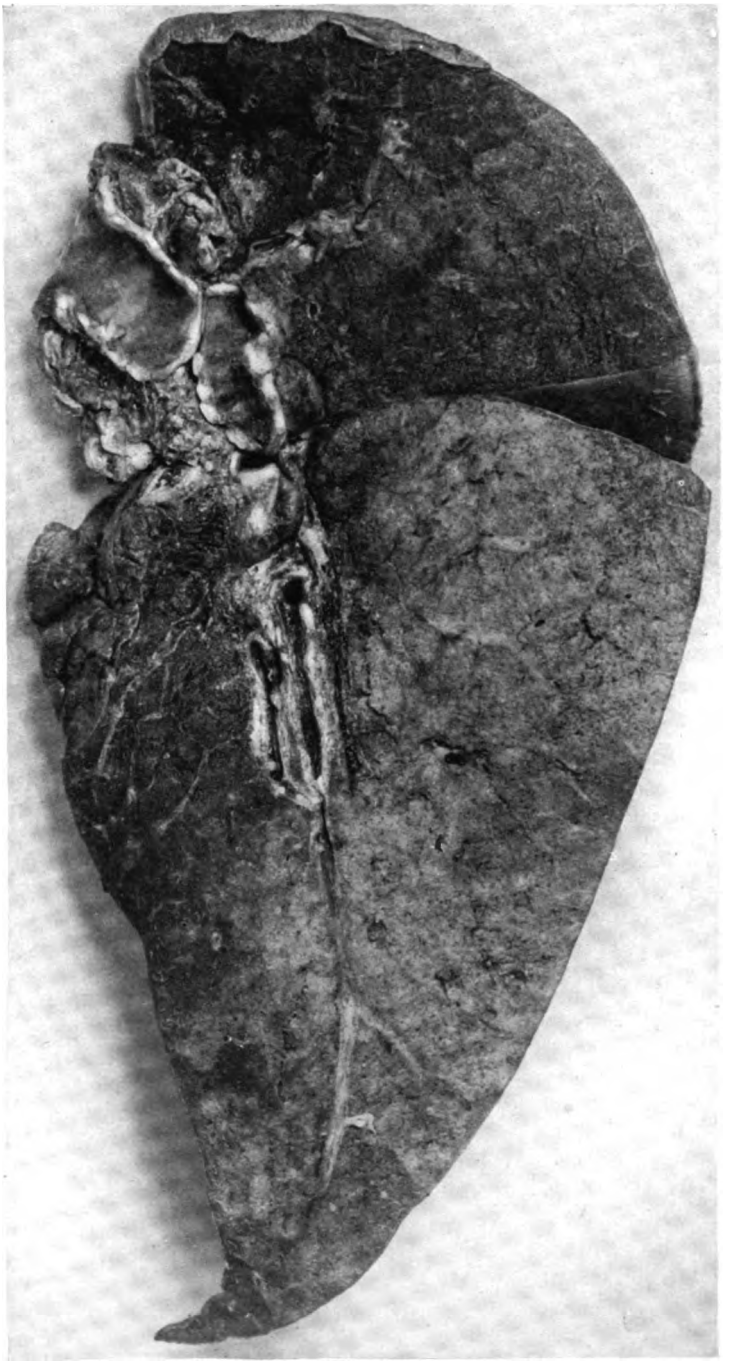

FIG. 13 (Case 228).—Right lung. Advanced confluent lobular pneumonia assuming practically lobar extent. *Pneumococcus IV and small Gram-negative cocci.*

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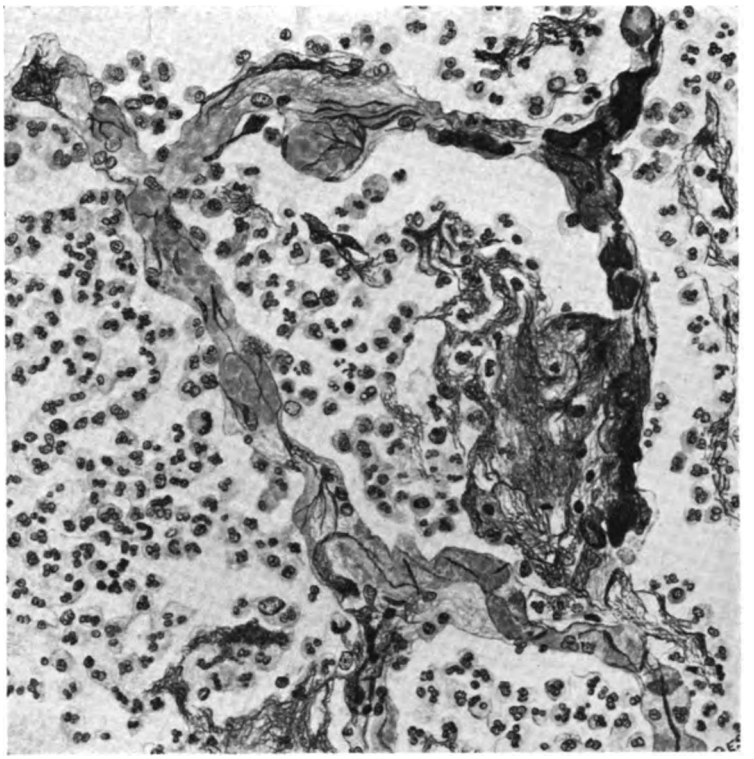

FIG 14 (Case 228).—Hyaline fibrinous thrombi of the capillaries of the alveolar wall with radiation of fibrin into the alveolar cavity.

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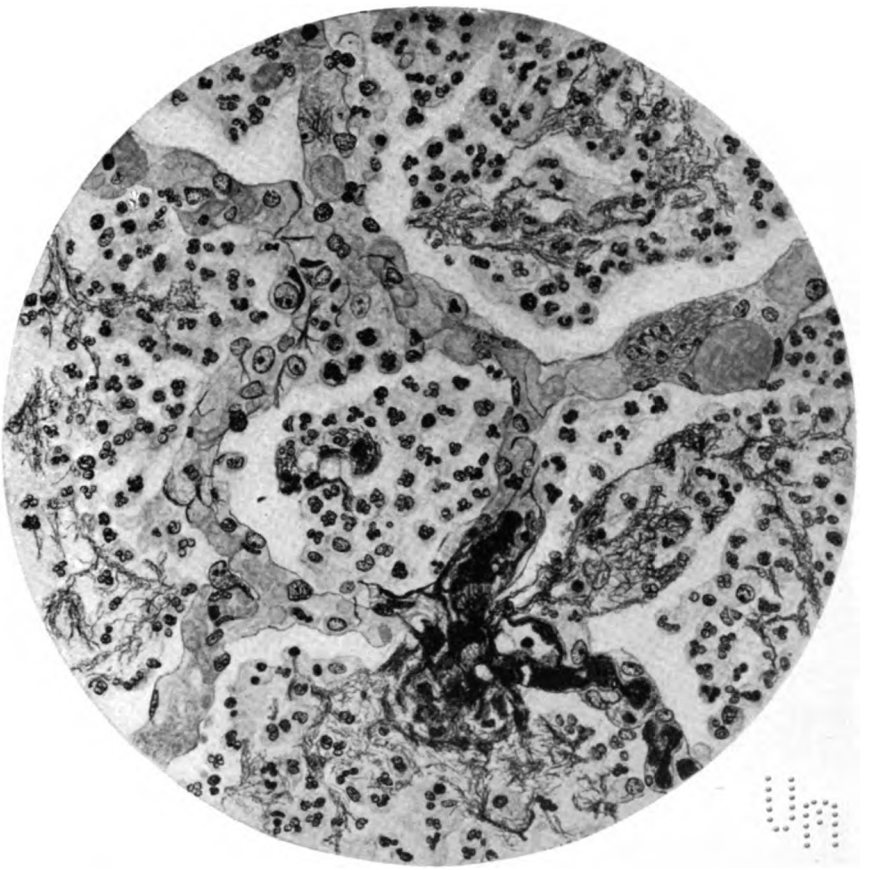

FIG. 15 (Case 228).—Another alveolus showing the obstruction of the capillaries in one area by hyaline fibrin.

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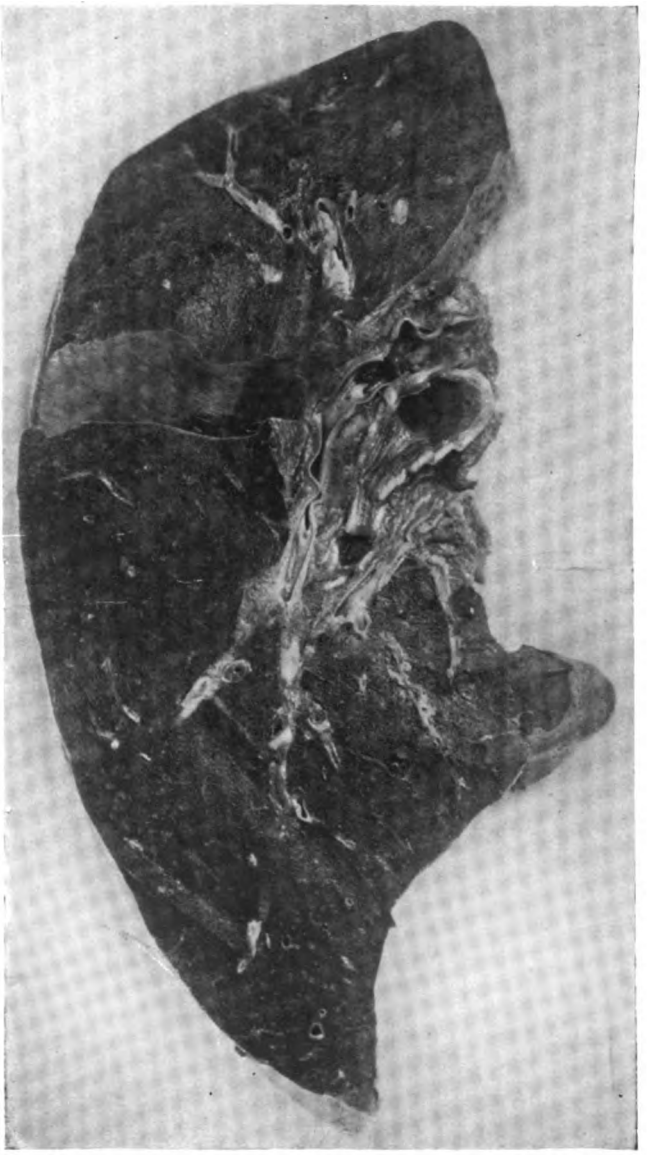

FIG. 16 (Case 214).—Left lung. Fresh hæmorrhagic pneumonic consolidation. *B. influenzæ.*

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FIG. 17 (Case 220).—Right lung. Peribronchial consolidation with extensive hæmorrhage. No bacteria found, but the lesion is comparable to that of Case 214.

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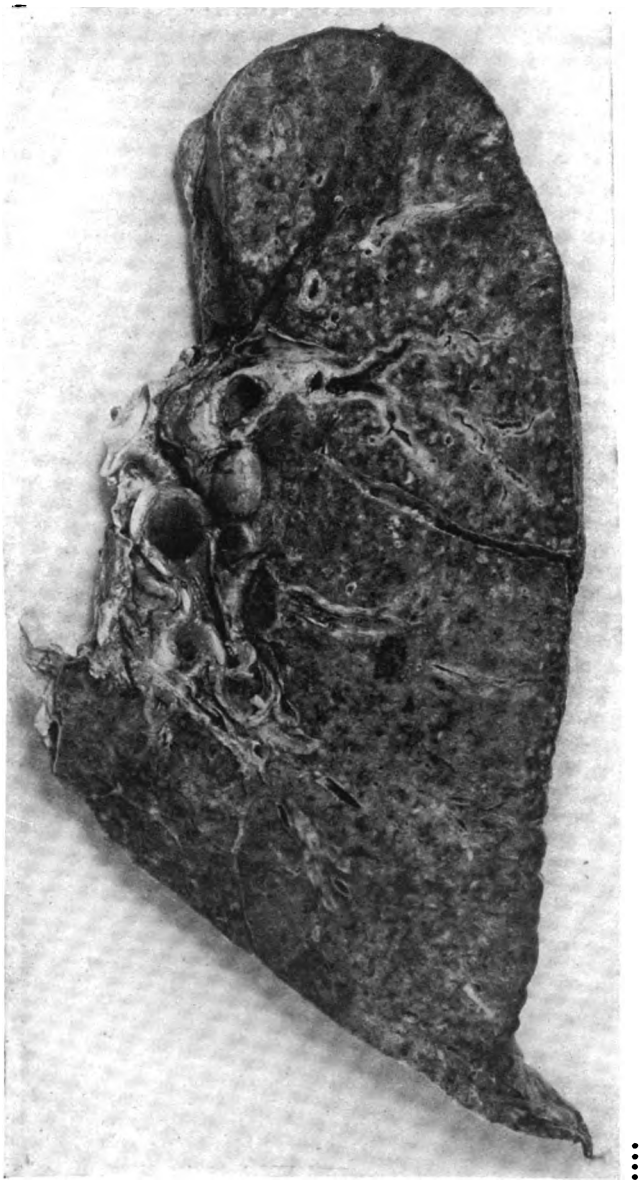

FIG. 18 (Case 81).—Right lung. Interstitial bronchopneumonia. *B. influenzæ.*

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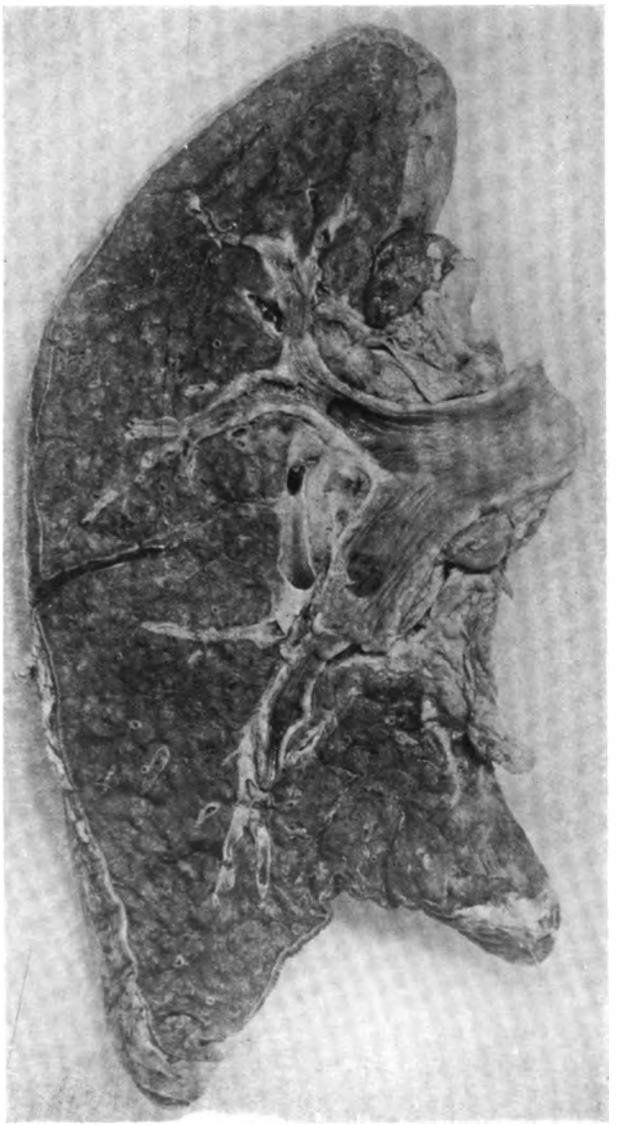

FIG. 19 (Case 81).—Left lung showing small prominent peribronchial nodules like tubercles.

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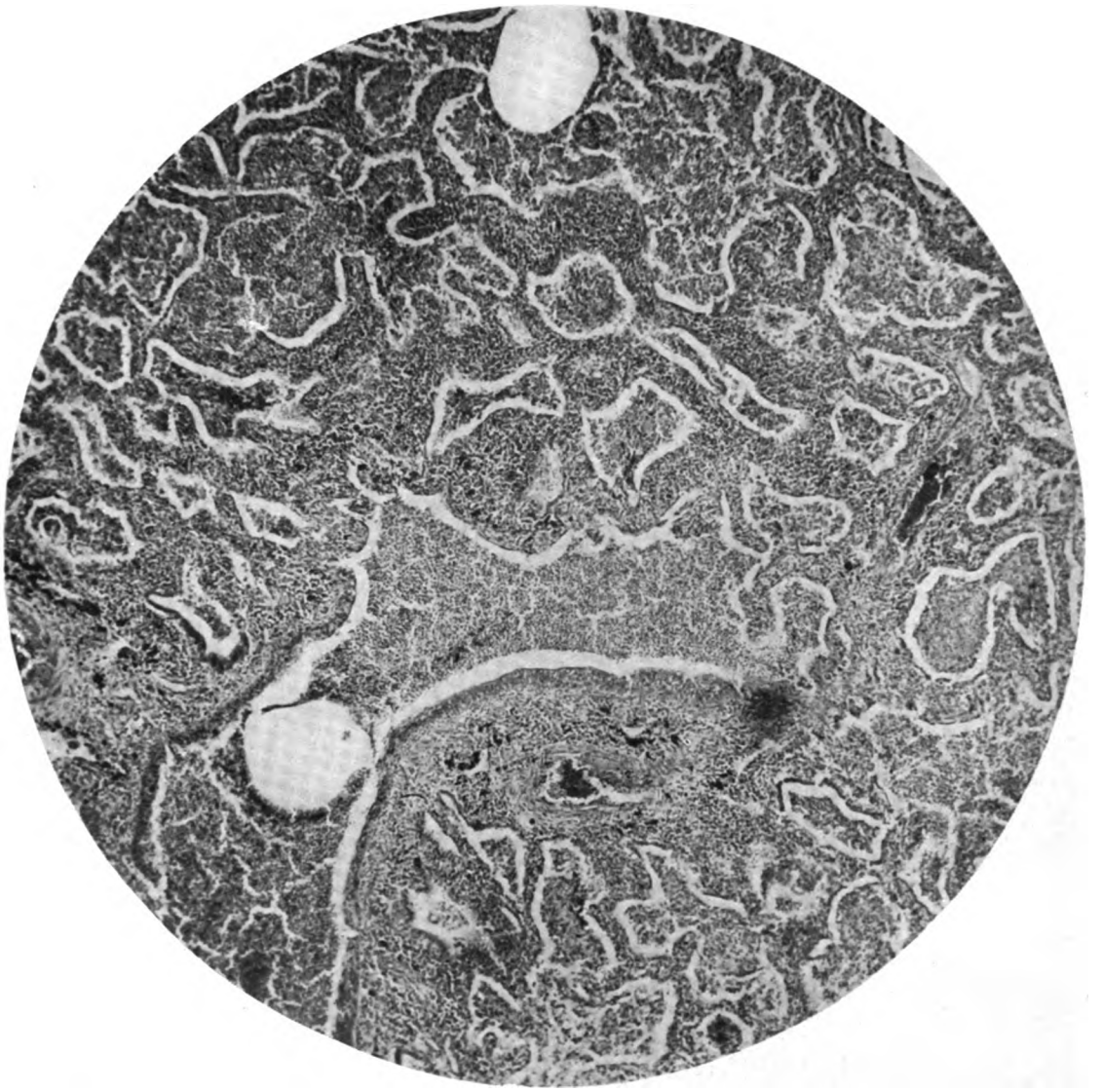

FIG. 20 (Case 81).—Right lung. Peribronchial infiltration and induration. *B. influenzæ*.

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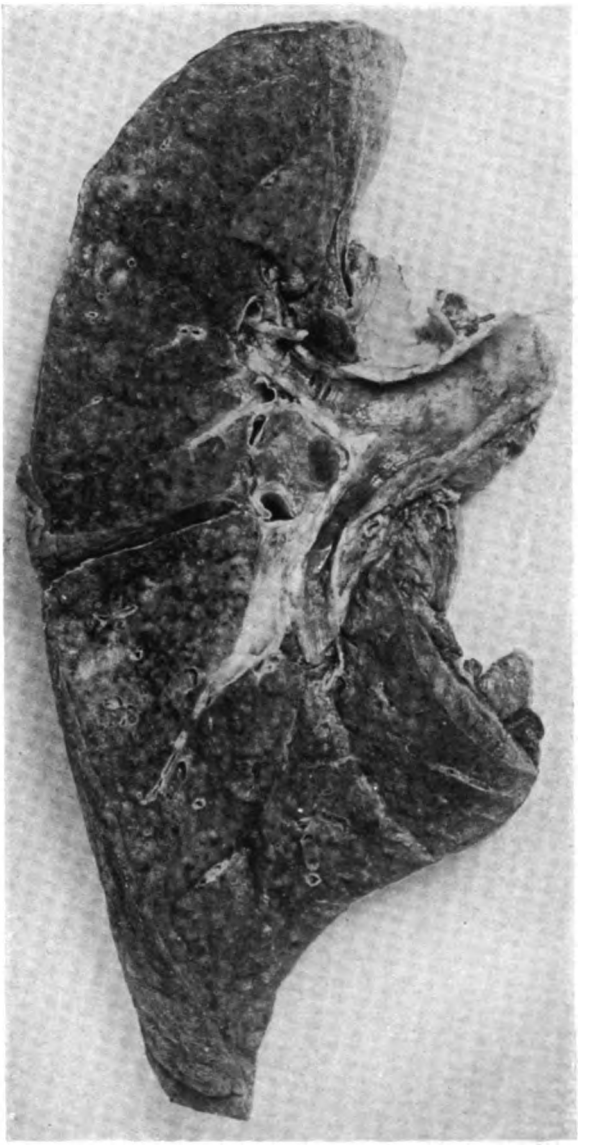

FIG. 21 (Case 86).—Left lung. Interstitial bronchopneumonia.

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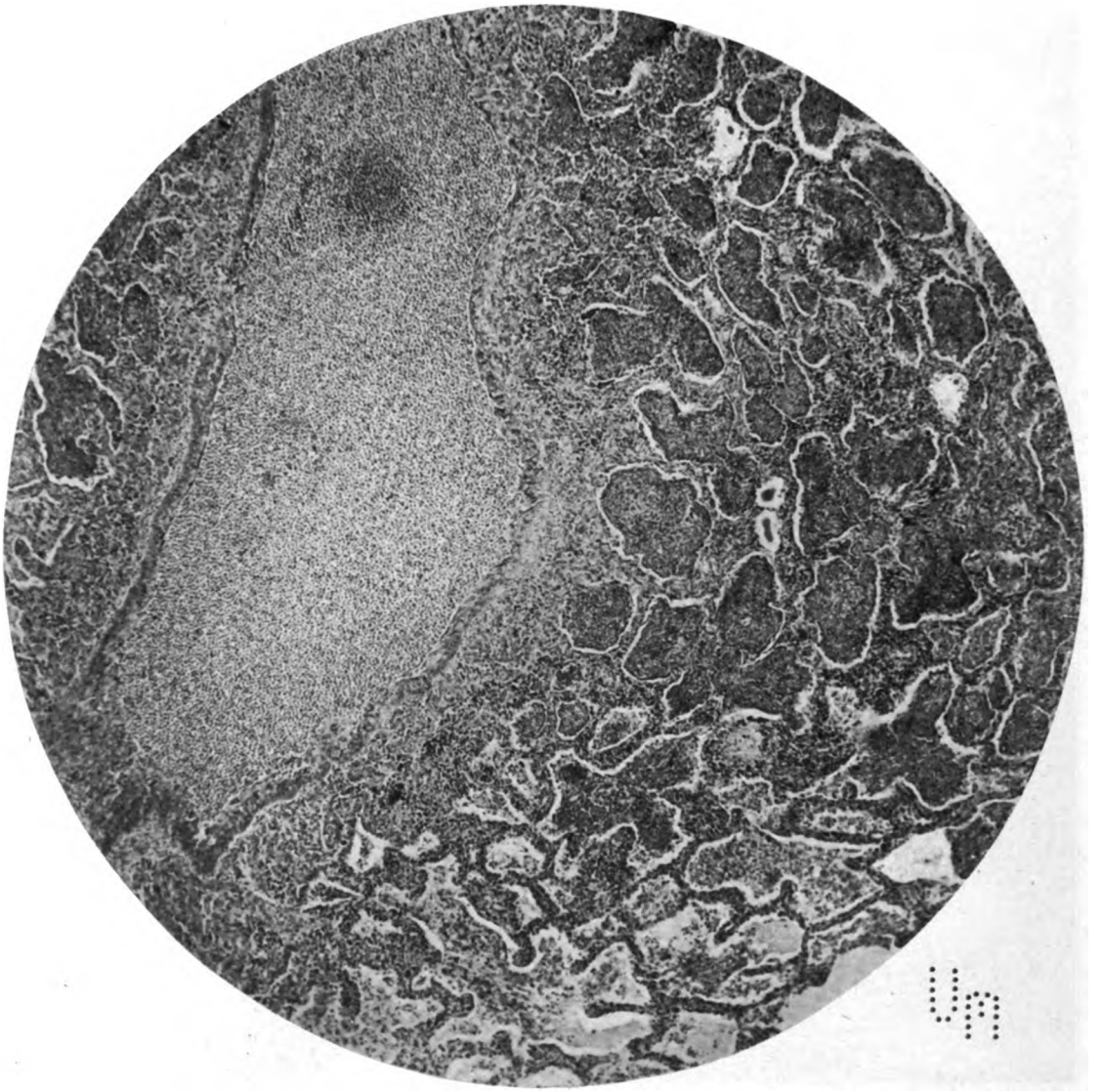

FIG. 22 (Case 86).—Thickening and infiltration of wall of bronchiole with peribronchiolar exudate and induration. *B. influenzæ.*

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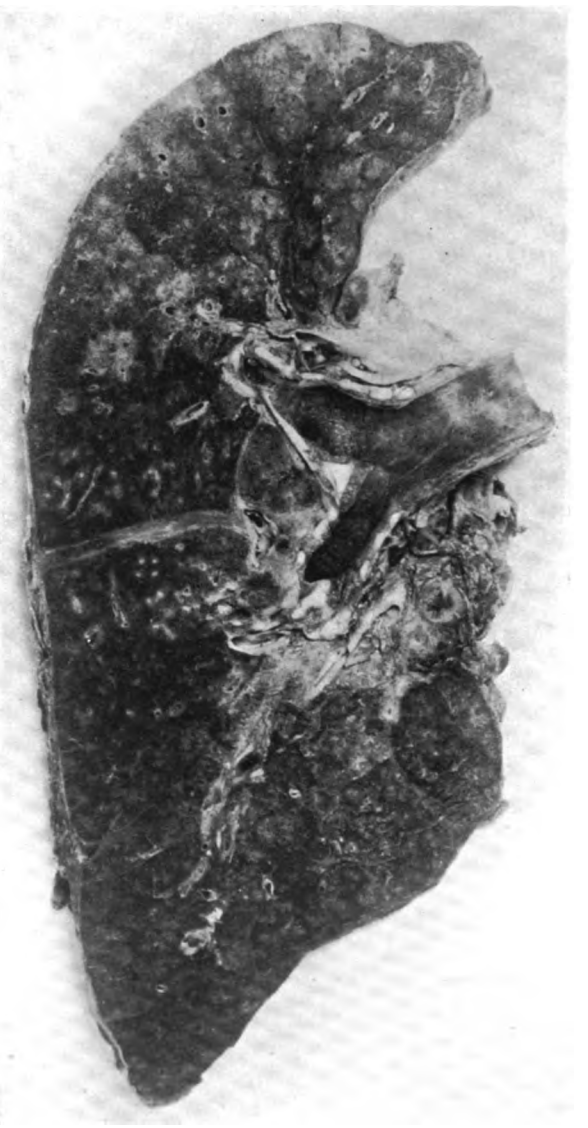

FIG. 23 (Case 89).—Left lung. Interstitial bronchopneumonia. *B. influenzæ.*

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LYMPHOSARCOMA. LYMPHATIC LEUKÆMIA. LEUCOSARCOMA. HODGKIN'S DISEASE

By L. T. WEBSTER

(Department of Pathology, The Johns Hopkins University, Baltimore, Md.)

In 1832, Hodgkin brought together a series of cases characterized by a general swelling of the lymph glands and spleen. Tuberculosis and leukæmia, as well as the disease which now bears his name, were probably included. Virchow (1845), describing splenic and lymphoid leuksæmia, sharply distinguished cases of glandular enlargement associated with an increase in the number of white blood corpuscles.

The large group remaining, unassociated with blood changes, has been discussed at length. Wilkes, in 1856, described a general disease of the lymph glands beginning in the neck and progressing to tumor formation of the internal organs associated with anæmia and cachexia. This condition he called lymphatic anæmia but later (1865) all cases of general glandular enlargement without leukæmia were called by him Hodgkin's disease. At about this time, Germans were reporting similar cases—Wunderlich (1858), Lambl (1860), Billroth (1861).

It remained for Virchow, however, in 1863, to offer the first intelligible classification based on previous case reports and his own observations. In brief, it is as follows:

1. Leukæmic lymphoma.

2. Simple hyperplastic lymphoma involving lymphoid tissue and spleen; transition stage between leukæmic lymphoma and lymphosarcoma.

3. Lymphosarcoma. Tumors consisting of simple hyperplasia of gland elements progressing in spite of all treatment. They approach leukæmic tumors at times, differing only by absence of blood picture.

(a) Soft form; proliferation of ordinary lymphoid cells.

(b) Hard form; great increase in connective tissue and recticulum. Finally lymphoid cells tend to disappear.

But what Wilkes in England had called Hodgkin's disease, and Virchow in Germany had called lymphosarcoma, was still to receive

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further labels. Trousseau, in 1865, after a most careful study, concluded that leukæmia and "l'adénie" were distinct affections with different etiology and course. After Wunderlich's excellent summary of cases (1866), Langhans (1872) comments on Virchow's classification and prefers the term "malignant lymphosarcoma." The soft form, according to him, is a disease of the entire lymphatic system frequently accompanied by infiltrations into the liver, kidneys, ovaries, and other organs. The hard form with decrease in lymphocytes, proliferation of reticulum and connective tissue, is histologically quite different. Birch-Hirschfeld and Langhans mention giant cells observed in the hard form.

We note then, as far back as 1863, the microscopic distinction between lymphoid hyperplastic conditions and reticulum-endothelial cell hyperplastic conditions. But Winiwarter (1875) and many others since his time have refused to accept two pathological entities and consider Virchow's hard and soft forms of lymphosarcoma as stages in the development of a single process.

From this Hodgkin's-lymphosarcoma-l'adénie group, Kundrat (1893) extracted a series of cases to which he gave the name, now in use, of "lymphosarcoma." According to his description, this disease originates from a single lymph gland or follicle, breaks through the capsule and invades locally by way of the lymphatics. No diffuse or nodular metastases in the liver or spleen occur; no bone marrow changes.

Still there continued to appear in the literature from time to time peculiar cases difficult to classify. Hutchinson reports a lymphoid tumor in a 19-year old boy which involved subcutaneous tissue, brain, retroperitoneal fascia, as well as lungs, intestine, kidneys, and mesenteric glands. The W. B. C. were "slightly increased." Heddon describes a 14-pound abdominal tumor of the mesenteric glands associated with general glandular enlargement and infiltration of liver and spleen. Cohnheim (1865), using the term "pseudoleukæmia," described a case where gross and microscopical findings resembled leukæmia but which lacked the characteristic blood changes. And again, Goppert's case (1896), that of a three-year old child who had at autopsy lymphoid tumors of kidney, thymus, inguinal and retroperitoneal glands, with infiltration of spleen, liver, and bone marrow, is another example of the many bizarre pictures observed in this group.

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From Virchow's hard form of lymphosarcoma with its addenda by Langhans, Winiwarter, Birch-Hirschfeld, and others, D. Reed, in 1902, crystallized the conception of "a pathological entity, the main features of which are painless progressive glandular enlargements, usually starting in the cervical region, without the blood changes of leukæmia. The growth presents a specific histological picture consisting of proliferations of the reticular and endothelial cells, formation of lymphoid cells, characteristic giant cells, and a gradual increase of connective tissue, resulting in fibrosis. The microscopical examination is sufficient for the diagnosis."

Finally, Sternberg, in 1908, differentiated a number of cases characterized by tumor growths of different organs and a leukæmia of a large lymphocyte type. To this group he gave the name "leukosarcoma."

Nothing has been added to clear our confused ideas since 1908. Hirschfeld and Kaufmann believe that lymphosarcoma may be localized or general, involving the entire lymphatic apparatus. Hesse would include, under the term "aleukæmic lymphadenosis," all types of lymphosarcoma, local or general, and adds that between lymphatic leukæmia and aleukæmic lymphadenosis there is a gradual but no essential difference. This latter relationship has been urged by Hirschfeld, Ribbert, and Baumgarten, and an explanation has been offered by Pappenheim, who says that if the disease-causing agent attacks the bone marrow, lymphoid leukæmia results, if it attacks the glands, lymphosarcoma is the consequence.

What then is the present status of this group of diseases and is it possible, without direct experimental etiological studies, to simplify the classification and to eliminate a part of the existing confusion?

To-day, under the term "lymphatic leukæmia," it is customary to include all cases with a permanent increase in the lymphocytes of the blood associated with a hyperplasia of the lymphoid tissue. Cases of general glandular enlargement, infiltration of parenchymatous organs and bone marrow but no clinical blood changes (pseudoleukæmia), as well as cases of leukæmia associated with an invasive tumor (leukosarcoma), are usually wedged into this group. "Lymphosarcoma" has so far lost the meaning ascribed to it by Kundrat that it seems to include everything from his strictly localized invasive tumor to such a case as has been recently described by Schnyder. It concerned a white male, aged 17 years, who three weeks before death developed

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pains in his back, dyspnœa, and weakness. The blood count showed a leucocytosis of 12,300 with P. M. N. 69 per cent, and L. 13 per cent. Autopsy showed an invasive tumor of the mediastinum and pleura with involvement of lymph glands, adrenals, kidneys, liver, gall bladder, dura mater, femur, tonsils and tongue follicles. In other words, we have returned to Virchow's idea of the soft form of lymphosarcoma. Hodgkin's disease, Virchow's hard form of lymphosarcoma, sharply defined by Reed and Ziegler, is usually considered to be an entity. But the ever-increasing "intermediate forms and transitional stages" between lymphatic leukæmia and lymphosarcoma and between lymphosarcoma and Hodgkin's disease increase beyond reason the power of the personal equation.

TABLE ILLUSTRATING PRESENT CLASSIFICATION

Lymphatic Leukæmia	←	Lymphosarcoma		Hodgkin's Disease
(a) Typical		(a) Local (Kundrat)	↑	(a) Typical
↑↓ (b) Atypical blood picture (Pseudoleukæmia)		↓ (b) General		↑ (b) Transitional
↓ (c) Invasive tumor (Leukosarcoma)				

So much for the present status of this group. It remains now to describe a number of cases of leukosarcoma, lymphosarcoma, lymphatic leukæmia, and Hodgkin's disease, discuss them, and propose a more simple classification.

Leukosarcoma

Leukosarcoma was used by Sternberg to designate a group of cases characterized by a leukæmic blood picture and an invasive lymphoid tumor. The origin of this tumor, neoplastic in nature, might be anywhere—breasts, skull, mediastinum. The blood picture is not that of a small lymphocytic leukæmia but shows a high percentage of large lymphoid or "leukosarcoma" cells. Helly apparently goes further by differentiating leukosarcoma (a true neoplastic tumor) according to its association with "lymphopænia, sublymphæmia, or lymphæmia." On the other hand, Türk and Naegeli believe that leukosarcoma is only a stage of lymphatic leukæmia.

I will describe four cases taken from the autopsy records of The Johns Hopkins Hospital and will summarize 22 cases collected from the literature. From this study, it may be possible to derive a more

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precise knowledge of the clinical course and pathology of this group and to discuss more accurately its relationship with allied conditions.

CASE 1.—Early D., black, male, age 23. Family history and past history negative. Present illness: Onset four months before admission with lumps on sides of neck increasing in size. One month ago the patient noticed lumps in inguinal region. About two weeks before admission, anorexia and weakness became marked. Physical examination, January 4, 1902, showed full abdomen in which the spleen was palpable about 6 cm. below the costal margin. Liver extended 3 cm. below the costal margin. The glands of the neck were all enlarged, firm and discrete. Submental glands were enlarged, axillary, epitrochlear, and inguinal glands were greatly enlarged; tonsils were swollen. R. B. C. 5,230,000. Hb. 85 per cent. W. B. C. 33,000. Differential P. M. N. 21.8 per cent, S. and L. mono. 76 per cent, eosinophiles .8 per cent, transitionals .6 per cent. Course in hospital: On January 18 a lymph gland removed for diagnosis showed a stroma filled with round vesicular nucleated cells, some showing mitotic division. These cells are larger than lymphocytes. Lymphatic leukæmia and a general sarcoma of the lymph glands were considered. On January 25 patient vomited considerably, the lymph glands appeared slightly larger, fever disappeared, and the blood condition remained about the same. February 6-10, œdema of thighs had developed, extending over face and trunk; the abdomen was much distended. March 12, two litres of fluid were aspirated from the abdomen. Specific gravity 1.019; alkaline; albumin 30 gm. per litre. The cells were mostly mononuclears. March 14, patient's abdomen was tapped again and 1 litre of a similar fluid was removed. April 11, general anasarca developed, dyspnœa and weakness continued, and the patient died at 1 p. m. April 15.

BLOOD CHART WHILE IN THE HOSPITAL

Date.	R. B. C.	Hb.	W. B. C.	P. M. N.	S. M.	E.	T.
1-4-02	5,220,000	85%	33,000	21.8%	76%	.8%	6. %
1-13-02	5,600,000	66%	23,000	.....	....	....	....
2-2-02	5,224,000	54%	2,750	44. %	41%	6.6%	5.2%
2-12-02	4,224,000	54%	2,375	55.9%	38%	2.4%	.7%
3-21-02	4,105,000	55%	3,540	75.7%	20%	.5%	2.6%
4-11-02	4,588,000	....	4,000	74.0%	21%	2.8%	.4%

Autopsy 1903. *Anatomical Diagnosis.*—Leukosarcoma; enlargement of the cervical, bronchial, mediastinal, retroperitoneal, pelvic and inguinal lymph glands; enlargement of lymph follicles of small and large intestines; hypertrophy of spleen; œdema of lungs; general anasarca.

Body.—Is that of a well nourished colored man 180 cm. long. Anasarca is marked. Submaxillary, cervical, axillary, and inguinal glands are enlarged. The peritoneal cavity contains a large amount of bloodstained fluid. The mesenteric lymph glands are enormous, some reaching the size

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of apples. They are soft and on section show a homogeneous red surface. The pelvic, inguinal, iliac and retroperitoneal glands form a continuous mass of small and large nodules. The right pleural cavity contains a large amount of blood-tinged fluid. *Heart:* Normal. *Lungs:* Old adhesions. The glands at the hilum are much enlarged and matted together. *Spleen:* 1320 grams. On section the cut surface is of a grayish-red color mottled with deep hæmorrhagic points, which are surrounded by white foci. *Liver:* Is also large, weighing 2700 grams. Lobules are easily seen. No nodules are visible. *Kidneys:* Are large, weighing 500 grams each. No nodules. *Adrenals* and *pancreas:* Normal. *Gastro-intestinal tract:* Appears normal except for numerous pigmented spots surrounded by white rings which appear in the large intestine; these are evidently solitary lymph follicles. *Glands:* A large mass measuring about 10 x 4 cm. is found directly beneath the under part of the sternum, distending the upper part of the pericardial sac. On section this mass appears œdematous and of a uniform soft consistency. The position of this mass suggests a large persistent thymus. The substernal glands are much enlarged and of similar appearance on section. *Tonsils:* Are enlarged and deeply pigmented; they form projections as large as walnuts on either side of the epiglottis. *Bone marrow:* Is of a deep red color and of a jelly-like consistency. The remainder of the autopsy is normal.

Microscopic Pathology.—Tumor: Sections show a homogeneous, cellular tumor of the lymphoid type. The cells are arranged in columns and chains supported by a delicate, though obvious, stroma. They are regular in size (4-6μ) and quite regular in shape. Cytoplasm is scant; nuclei are deeply staining and show a few coarse chromatin granules. No mitotic figures are seen. *Posterior auricular gland:* Shows on section a thickened, intact capsule surrounding a homogeneous mass of lymphoid cells which obliterate entirely the normal architecture. No germinal centers are seen; sinuses, very indistinct, are filled with lymphocytes. These cells appear quite as those described above, small, regular, not especially precocious in growth or activity. *Spleen:* Shows intact capsule and trabeculæ. Malpighian bodies are obscured by the general infiltration of lymphoid cells similar to those seen in the tumor. *Liver:* No material. *Kidneys:* Sections unsatisfactory. *Intestines:* Lymphoid cells are scattered diffusely throughout the mucosa and submucosa. *Bone marrow:* The cells are reduced in number and are accompanied by a diffuse infiltration of lymphoid cells.

Briefly, a colored man, aged 23 years, came to the hospital with a four months' history of rapidly growing tumor masses in the cervical region, anorexia, and dyspnœa. Physical examination, January 4, 1902, disclosed a general glandular enlargement, ascites, large spleen and liver. R. B. C. 5,230,000, Hgl. 85 per cent, W. B. C. 33,000. Large and small mononuclears 76 per cent. An excised lymph gland was diagnosed lymphatic leukæmia or possible "general sarcoma of

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lymph glands." The patient ran an acute course developing generalized œdema, recurrent ascites, and died three and a half months after admission. During this period, a secondary anæmia developed. W. B. C. dropped from 33,000 to 2,375; P. M. N. rose from 21.8 per cent to 74 per cent, while the large and small mononuclears dropped from 76 per cent to 21 per cent. Autopsy revealed a general glandular enlargement, an infiltration of parenchymatous organs and bone marrow, and a large invasive tumor of the mediastinum. Everywhere the cells were of the lymphoid type, regular and similar in size (4-6 μ.) and shape and general morphology.

So one might regard this case, with a total duration of seven and one-half months, as lymphatic leukæmia associated with an invasive tumor; that is, a "leukosarcoma."

Case 2.—No name, white, male, age 7. The history is incomplete, but the onset evidently began four months before admission with dyspnœa and oppressive chest symptoms. At the time of examination, general glandular enlargement was made out and a large spleen palpated. The leucocytes numbered 230,500, with a predominance of small lymphocytes. The child became weaker and died three months after examination

Autopsy 2111. *Anatomical Diagnosis.*—Leukosarcoma filling the chest, invading pectoral muscles, parietal pericardium and parietal pleura; extension along hilum of lungs; enlargement of all lymph glands of body; large spleen; red bone marrow; emaciation.

***Body:* Is that of an emaciated boy. The cervical, axillary, inguinal and mesenteric glands are large and firm. Infiltrating the pectoral muscles is a soft grayish tissue which seems to come from the chest cavities after penetrating the pleura. A tumor measuring 18 cm. x 15 cm. x 9.5 cm. occupies the mediastinum beginning at the clavicles above, filling the left pleural cavity, and extending as far as the costal angle. It is adherent to the sternum and diaphragm and to all the structures that rest upon the bodies of the vertebræ. Sheets of tumor extend from the hilum of the lung out over the posterior half of the parietal pleura. Its consistency is soft and on section presents a raised, moist, uneven appearance with areas of hæmorrhage and degeneration. The heart is completely enclosed in the tumor mass which is in intimate and inseparable relation with the pericardium. *Heart:* Normal. *Lungs:* Partly atelectatic. *Spleen:* Weighs 400 grams. On section it appears soft and of a deep reddish brown color. The Malpighian bodies are inconspicuous. *Liver:* Large. No nodules found. *Kidneys:* Each organ shows a solitary wedge-shaped nodule projecting from the surface. *Pelvic organs, gastro-intestinal tract, pancreas, adrenals:* Seem clear. *Retroperitoneal glands:* Especially at the hilum of the liver, are very large. On section they appear soft. The glands along the region of the pelvis and the inguinal glands present the same appear-**

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ance. *Bone marrow:* Soft and jelly-like, homogeneous and bright red in appearance.

Microscopic Pathology.—Tumor mass: Sections show a cellular tumor of the lymphoid type. Stroma is composed of a delicate network of reticulum cells. Blood vessels are not conspicuous. Tumor cells grow thickly and uniformly, forming the entire structure. In size, they are quite regular, averaging 4-5½μ in diameter. Usually, no cytoplasm is visible. Nuclei are quite uniform. Most of them are circular, deep staining with several coarse chromatin granules. *Gland:* Appears as solid tumor mass. Lymphoid cells invade the pericapsular fat. All architecture completely changed by the homogeneous mass of lymphoid cells which masks completely all evidence of sinuses and germinal centers. The cells resemble precisely those described above. Blood vessels contain these cells. Trabeculæ are not conspicuous. *Liver* and *spleen:* Show lymphoid infiltration with few wandering cells. *Bone marrow:* The marrow cells are reduced in quantity. Lymphoid cells are numerous and the large cells mentioned above are seen. R. B. C. are present in usual amount.

The history in this case is meagre. A white boy, 7 years old, was seen in consultation after a four months' history of dyspnœa and oppressive chest symptoms. Examination disclosed a general glandular enlargement with enlarged spleen. W. B. C. numbered 230,500 "with a predominance of small lymphocytes." Seven months after onset the child died. Autopsy revealed a general glandular enlargement, an infiltration of parenchymatous organs and bone marrow, and a large, invasive tumor of the mediastinum filling the chest, invading the parietal pericardium, pleura, lungs and pectoral muscles. Everywhere the cells were of the lymphoid type, regular and similar in size (4-6 μ), shape and general morphology.

One might regard this case, too, with a total duration of seven months, as lymphatic leukæmia associated with an invasive tumor; that is, a "leukosarcoma."

CASE 3.—Albert M., white, male, age 28. Family history and past history unimportant except that for two years he had noticed a heavy feeling over the chest. Present illness began five months before admission with progressive enlargement of neck, dyspnœa, cough, dysphagia and orthopnœa. Examination December 3, 1918, showed cough, dilated veins over the upper chest and face, palpable hard lymph glands in lower neck, right and left sides, axillæ and episternal notch. There was retromanubrial dulness and a tracheal tug. Liver and spleen were palpable. The Wassermann was negative; the urine was negative; X-ray reported a large mass in the mediastinum which suggested either Hodgkin's or lymphosarcoma.

Course in hospital. December 19 (two weeks after admission) his dyspnœa, dysphagia and cough became worse. Insomnia developed, the

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	December.				January.								
	4	11	17	31	7	9	10	11	12	14	15	16	17
R. B. C.	4,272,000	4,480,000	4,576,000		3,548,000	3,516,000	2,926,000	3,088,000	2,912,000	3,680,000	3,752,000	3,192,000	3,384,000
Hgl.%	80	82	80		68	64	56	56	53	58	60	56	56
W. B C.	3,960	5,080	5,200	31,000	87,400	46,800	33,200	38,920	40,680	37,840	37,840	13,320	11,400
P. M. N.%	59	56	67	X-Ray treatment Dec. 19–23 Jan. 6 Hemorrhage Thoracentesis 200 c.c.	0	4	3	2	2	2	6	7	5
P. M. E.%	1	1	2		0	0	0	0	0	0	½	0	1
P. M. B.%	½	0	1		0	0	0	0	0	0	½	0	½
L. %	25	25	20		41	42	47	58	40	34.3	42	31	36
L. M.%	6½	5	3		2	3.3	0	0	0	0	1½	0	1½
T.%	7½	12	7		0	3.3	.3	0	0	0	0	0	½
Myelocytes%	0	1	0		0	0	0	0	0	0	0	0	0
Smudges%	0	0	0		57	47.4	49.7	40	58	63.7	49½	62	55½

Transfusion 250 c.c. Transfusion 500 c.c. Transfusion 600 c.c. Thoracentesis 1200 c.c. blood Transfusion 300 c.c.

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venous dilatation and suffusion became more marked on the right side than on the left. Anisocoria developed, more marked on the right side. The right radial pulse became more marked than the left radial. December 19-28, application of Coolidge tube over the chest one-half hour daily resulted in subjective improvement with reduction of dyspnœa and cough. However, with this, ecchymoses and petechiæ developed abundantly and rapidly. Epistaxes were frequent. Twitching pains in the "ham string" muscles became marked, with irregular fever. The X-ray treatment was discontinued. December 28—January 7, hæmorrhagic tendency increased. The tonsils, gums and mucous membranes of the nose have bled almost continuously. Petechiæ are seen over the entire body. 200 c. c. of bloody fluid were aspirated from the left pleural cavity. (R. B. C. 1,600,000.) All the lymph glands have enlarged markedly, are soft and tender, and fever has become continuous. January 7-18, respirations have become accelerated, the pulse weak and thready. Irregular rises in temperature have occurred, and hæmorrhage has been marked. During this period four transfusions were administered totalling 1650 c. c. After the third transfusion 600 c. c. of blood were removed from the left chest. January 18, death.

Autopsy 5798. *Anatomical Diagnosis.*—Leukosarcoma of mediastinal lymph glands extending into pericardium, diaphragm and left parietal pleura; lymphocytic infiltrations of spleen, pancreas, liver, kidneys and bone marrow; general glandular enlargement; left hemothorax with collapse of left lung.

Body: Is that of a medium-sized young man 160 cm. long, weighing 49 kilos. Rigor and livor mortis are marked. Tonsils are enlarged, submaxillary and all the cervical chains, axillary and inguinal lymph glands are palpable and soft. Petechiæ are numerous over the flexor surfaces of the arms, chest and abdomen. An extensive bluish discoloration is noted under the skin over the lower left side of the thorax. On opening the peritoneal cavity the liver edge extends 10 cm. below the xiphoid in the mid-sternal line. The spleen is 9 cm. below the costal margin. On opening the chest cavity a soft tumor mass is cut away from its attachments to the sternum. The left pleural cavity contains about 1½ litres of fluid blood and the left lung is completely collapsed. A soft mass of enlarged confluent mediastinal glands is forming a tumor which surrounds the blood vessels and bronchi and trachea and extends over the pericardium, forming a thick encasement for the heart. It extends over the diaphragm and left parietal pleura as a soft velvety membrane about 1 cm. in thickness. The cut surface of the lymph glands shows a homogeneous white cellular growth ignoring the capsule and obliterating all normal morphology. Hæmorrhagic areas are seen. These glands, particularly at the bifurcation of the trachea, are pressing firmly against the air passages and large blood vessels. Elsewhere in the chest the tumor shows the same soft, white, cellular masses growing freely over the serous surfaces. *Heart:* Normal. *Lungs:* The left lung is collapsed; the right lung is normal. *Spleen:* Weighs 590 grams.

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It is large and pale, rather firm in consistency. On section light bluish infiltrations stand out against the deeper colored background. The Malpighian bodies cannot be seen. *Pancreas:* Is encroached upon by large retroperitoneal glands. On section fatty infiltration, tumor growth and opaque white nodules are seen throughout the tissue. *Liver:* Weighs 2440 grams. It is large and pale. On section the cut surface shows normal liver lobules with lighter areas in which no lobulation is evident. *Adrenals:* Normal. *Kidneys:* Are large and pale. On section numerous homogeneous, opaque white nodules stand out as elevations on the kidney surface, throughout the cortex and pyramids. Striæ and glomeruli are widely separated. *Pelvic organs:* Normal. *Retroperitoneal glands, lumbar glands* and *axillary glands:* Are all very much enlarged, soft, and on section present an appearance identical to that seen in the bronchial glands. *Neck organs:* Tonsils and all cervical glands greatly enlarged. *Intestines:* Show hypertrophy of all lymphatic tissue.

Microscopical Notes.—Tumor: Is composed of a solid mass of lymphoid cells supported by a delicate stroma. The cells are uniformly distributed; regular in size (6-7μ) and shape. The nuclei are somewhat vesicular. Many mitoses are noted. Blood vessels are quite numerous. *Gland:* Appears as a homogeneous mass of lymphoid cells. The capsule and surrounding fat are invaded. The normal architecture is obscured, sinuses and germinal centers usually cannot be determined. A few distorted sinuses near the capsule are crowded with lymphoid cells. These cells which seem to form the entire gland are regular in size (5½μ) and shape. Cytoplasm is scant. Nuclei are rather vesicular and contain many coarse chromatin granules. Many mitotic figures are present. *Spleen:* The capsule and trabeculæ are normal. The homogeneous infiltration of lymphoid cells throughout the pulp obscures the Malpighian bodies. No normal lymphocytes are present. *Liver:* Shows portal accumulations of lymphoid cells similar to those described above. They are sifting into the lobules between the hepatic cells. *Kidneys:* Each glomerulus and tubule is separated by lymphoid cells which sometimes occur as solid masses. They surround the larger blood vessels and infiltrate down into the pyramids. *Bone marrow:* Is packed with lymphoid cells almost to the exclusion of the other elements.

Briefly, a white man, aged 28 years, came to the hospital with a fours months' history of dyspnœa, cough, dysphagia, and with rapidly growing cervical tumors. Examination, December 3, 1918, disclosed glands in the chest, axillæ, and neck, enlarged spleen and liver. At this time, R. B. C. numbered 4,272,000, Hgl. 80 per cent, W. B. C. 3,960 and S. M. 25 per cent. An excised gland from the neck was diagnosed lymphosarcoma. X-rays were applied daily from December 19-28. On December 31, the W. B. C. had increased to 31,000. A hæmorrhagic tendency developed acutely. The W. B. C. rose to 46,000 and dropped again to 11,400 just before death. S. M. rose to 58 per

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cent dropping to 36 per cent. General glandular enlargement developed with remarkable rapidity. Hæmorrhages continued and the patient died January 18, 1919. Autopsy revealed a general glandular enlargement, an infiltration of all parenchymatous organs and bone marrow, and a large, invasive tumor of the mediastinum. The invading cells were of the lymphoid type, regular and similar in size (4-6μ), shape, and general morphology.

The clinical course seems to be divisible into three main symptom groups: first, the period of mediastinal pressure symptoms (lymphosarcoma); second, leukæmic symptoms (acute lymphoid leukæmia); third, secondary anæmia symptoms resulting from hemorrhage. The autopsy finding of an invasive mediastinal tumor would tend to place this case in the "leukosarcoma" group.

CASE 4.—Audrey D., white, female, age 12. Family and past history are negative. Onset, June, 1919, with swelling of right parotid which disappeared in one week (mumps?). Two months later a dry, unproductive cough was noticed which persisted. Eyelids became puffy; glands of neck began to swell about one month ago; weakness and pallor developed rapidly. Examination, December 14, 1919, in the Harriet Lane Hospital, showed an emaciated, anæmic child, weak and coughing. General glandular enlargement, retromanubrial dulness, large spleen and liver noted. Pirquet and Wassermann were negative. Temperature 100°. X-ray showed mediastinal mass. Patient continued a downward course in the hospital and died December 20, 1919, six hours after her first radium treatment.

Date.	R. B. C.	Hb. %	W. B. C.	P.M.N. %	L. %	Smudges %	Myelocytes %	Nucleated R. B. C.
12–14	1,836,000	32	33,600	4	66.4	21.6	7.2	+
12–15	2,016,000	30	65,000	9.2	62.8	15	12.4	+
12–19	1,907,200	30	81,000	2.8	53.2	37.6	6.4	+

Autopsy 6096. *Anatomical Diagnosis:* Leukosarcoma involving mediastinum, thymus and lymph nodes, parietal pleura, pericardium and epicardium with resulting compression of esophagus, trachea, bronchi and mediastinal vessels. Leukæmic infiltration of liver, spleen, ovaries, kidneys, bone marrow, stomach and lymph nodes.

Body: Is that of a young girl weighing 16 kg. Pallor of skin and mucous membranes is marked. Tonsils are not enlarged. There is a marked general glandular enlargement including cervicals, axillaries, sublinguals, inguinals and epitrochlears. On opening the peritoneal cavity, the liver appears greatly enlarged. The mesenteric and retroperitoneal glands are prominent. The mediastinum is filled by a tumor mass occupying the entire

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anterior portion of the thoracic cavity. Pleural and pericardial surfaces show great thickening, especially the parietal pleura on the posterior wall. Here and over the diaphragm and pericardial sac it is dense and white, several times its normal thickness. The position of the thymus is taken up by a large white mass adherent to all adjacent structures. It shows no well defined limit. Included in this tumor are many enormous white lymph glands varying from 1 cm. to 3 cm. in diameter. *Heart:* Shows definite white infiltration at the apex beneath the epicardium, measuring 3-4 cm. in thickness. Otherwise, endocardium, valves and myocardium are quite normal. *Lungs:* At the hilum the lymph glands are enlarged and compress the neighboring thickened pleura. Lymphatics everywhere stand out prominently. *Spleen:* Weighs 160 grams. The pulp is soft and smooth. The Malpighian bodies are not conspicuous. *Mesenteric glands:* Along with the rest of the glandular system, are correspondingly enlarged, especially along the greater curvature of the stomach and near the cœliac axis. They are discrete. On section they show white, soft, glandular tissue, occasionally flecked with small hemorrhages. *Stomach:* Shows diffuse submucous infiltration producing a greatly thickened wall. *Liver:* Weighs 910 grams. Surface is pale and grayish brown. On section a diffuse infiltration of whitish areas are noted associated in and about the portal spaces. *Kidneys:* Are large (160 grams), pale, and firm. Scattered pinpoint hemorrhages are noted on the surface. The cortex averages 2 cm. in width and shows many small scattered hemorrhages. *Pelvic organs:* Are apparently not involved. *Lymph glands:* The inguinal glands are especially large and prominent. All others are moderately hyperplastic. *Neck organs:* Tonsils are not enlarged. The esophagus and trachea are compressed by the mediastinal mass. *Intestines:* Show no striking changes. *Bone marrow:* Dark red.

Microscopic Pathology.—Tumor: Appears as a homogeneous collection of lymphoid cells supported by a delicate reticulum. These cells, 5-8μ in diameter, are regular in size and shape, progressing from normal lymphocytes to pale vesicular mononuclears. Cytoplasm is scant. Nucleus contains coarse chromatin granules. Many mitoses are seen. *Heart:* The layer of endothelial cells surrounding the myocardium has been considerably displaced by great collections of lymphocytes. Large lymph vessels and small blood vessels are conspicuous. Superficial invasion of the lymphocytes between the muscle fibres occurs. *Pleura* and *diaphragm:* Show extensive lymphocytic infiltration. *Lungs:* Many of the alveoli are surrounded by collections of lymphoid cells. *Spleen:* The Malpighian bodies are not noticeably hypertrophied. They contain a few large cells in the center besides a peripheral accumulation of normal, small lymphocytes. The larger infiltrating lymphoid cells are scattered diffusely throughout the pulp. *Liver:* Shows an extensive periportal infiltration of lymphoid cells. Usually they are confined to the loose connective tissue forming Glisson's capsule, but occasionally they extend between the hepatic cells into the lobule. *Kidney:* Each glomerulus and tubule is surrounded by a mass of lymphoid cells, more numerous in the cortex, somewhat scattered

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and less frequent toward the pyramids. *Ovary:* The stroma in many areas is more or less replaced by collections of lymphocytes. *Stomach:* Shows lymphoid infiltration in the deeper layer of the mucosa. *Gland:* Appears as a homogeneous mass of lymphoid cells similar to those described above. All normal architecture is obliterated. *Tonsil:* Germinal centers are hyperplastic and seem composed of the larger lymphoid cells which are also filling homogeneously the entire substance of the tonsil. *Bone marrow:* An extensive lymphocytic infiltration obscures the normal bone-marrow cells. Megaloblasts are scattered about and occasionally small collections of myelocytes are seen.

Briefly, a girl 12 years of age came to the hospital with a six months' history of cough, glandular swelling, and progressive weakness. Physical examination, December 14, 1919, showed a general glandular enlargement, large spleen and liver with mass in mediastinum. Blood examination at this time showed a total number of W. B. C. 33,600 with lymphocytes 66 per cent and smudges 21 per cent. At the day of her death the W. B. C. had risen to 81,000, lymphocytes to 53 per cent, and smudges to 37 per cent. Autopsy revealed a general glandular enlargement, general infiltration of the parenchymatous organs and bone marrow, and a large invasive tumor of the mediastinum. Everywhere the cells were of the lymphoid type, ranging in size from the small lymphocyte (5μ) to the larger (7μ) pale mononuclear. This case might be regarded, with its duration of seven months, as lymphatic leukæmia associated with an invasive tumor; "leukosarcoma."

The cases taken from the literature have been summarized as follows:

Case 5.—Taylor (1873) reports a case of a patient 12 years of age who five weeks before admission developed œdema. Physical examination showed general glandular enlargement, enlarged spleen and liver. Duration ten weeks. Blood examination: definite increase in number of W. B. C. Autopsy showed a general glandular enlargement, tumor of the anterior mediastinum involving the pleura, infiltrations of liver, spleen and kidney.

Case 6.—Smith (1874) reports a case of a patient 30 years old who one month before admission developed an enlarged spleen and liver. Physical examination showed skin lesions over the chest. Great increase in number of W. B. C. Duration six months. Autopsy showed a general glandular enlargement, tumor of the anterior mediastinum infiltrating chest muscles, infiltration of parenchymatous organs.

Case 7.—Gowans (1876) reports a case of a patient 25 years old who three months before admission developed pleurisy, dyspnœa, and swelling of the glands. Physical examination showed a general glandular enlarge-

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ment, enlarged liver and spleen. Great increase in number of W. B. C. Duration five months. Autopsy showed a general glandular enlargement, tumor of the mediastinum involving pericardium, heart, blood vessels, and pleura, infiltrations of liver, spleen, kidneys and bone marrow.

Case 8.—Morison (1876) reports a case of a patient seven years old with a history of enlarged cervical glands, dyspnœa, and hæmorrhagic diathesis. Physical examination showed enlarged liver and a temperature of 105°. Autopsy showed enlargement of the cervical glands, an infiltrating mass in the mediastinum, involvement of the parenchymatous organs, and definitely leukæmic blood.

Case 9.—Turner (1879) reports a case of a patient 15 years old who three months before admission developed pains in arms and legs. Physical examination showed a general glandular enlargement, increase in size of liver and spleen, a hæmorrhagic diathesis, leukæmic blood, and high temperature. Duration four months. Autopsy showed a general glandular enlargement, an infiltrating mass in the anterior mediastinum and infiltration of the parenchymatous organs.

Case 10.—Packard (1891) reports a case of a patient six months old who four months before admission developed lumps on his back, head and feet. W. B. C. numbered 30,000. Duration five months. Autopsy showed a mass in the mediastinum, infiltration of the parenchymatous organs, and numerous skin nodules.

Case 11.—Dreschfeld (1891) reports a case of a patient 23 years old who three months before admission developed thoracic symptoms of oppression. Physical examination showed a blood picture of lymphoid leukæmia. Duration three and a half months. Autopsy showed a general glandular enlargement, a tumor mass in the mediastinum and infiltration of the parenchymatous organs.

Case 12.—Palma (1892) reports a case of a patient 18 years old who three months before admission developed chest symptoms. Physical examination showed general glandular enlargement and palpable liver and spleen. At this time the blood examination was practically normal. Two months later, however, the W. B. C. had risen to 372,000, and lymph glands, liver and spleen had enlarged tremendously. Duration five months. Autopsy showed general glandular enlargement, tumor mass in the mediastinum and an infiltration of the parenchymatous organs.

Case 13. Leader (1906) reports a case of a patient 11 years old who two months before admission became emaciated and developed enlargement of the cervical glands. Physical examination showed a general glandular enlargement and palpable liver. The blood showed a picture of lymphoid leukæmia. Duration four months. Autopsy showed a general glandular enlargement, tumor mass in the anterior mediastinum and infiltration of the parenchymatous organs.

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Case 14.—O'Kelly (1914) reports a case of a patient 19 years old who one month before admission developed a general weakness and malaise. Physical examination showed enlarged inguinal glands and spleen, a stomatitis, fever, and leukæmic blood. Duration one and a half months. Autopsy showed general glandular enlargement, tumor mass in the mediastinum and infiltration of the parenchymatous organs and bone marrow.

Case 15.—Sternberg (1915) reports a case of a patient 24 years old who four months before admission developed respiratory difficulty. Physical examination showed leukæmic blood. Duration five months. Autopsy showed general glandular enlargement, a large mass in the mediastinum, and an infiltration of the parenchymatous organs.

Case 16.—Sternberg (1915) reports a case of a patient 19 years old who three weeks before admission developed respiratory difficulty. Examination of the blood showed leukæmia. Autopsy showed a tumor of the mediastinum, general glandular enlargement, infiltrations of the parenchymatous organs and bone marrow, and numerous hemorrhages.

Case 17.—Sternberg (1915) reports a case of a patient 16 years old who three weeks before admission developed respiratory difficulty. Physical examination showed a tumor over the sternum and leukæmic blood. Duration four months. Autopsy showed a general glandular enlargement, tumor of the anterior mediastinum and infiltrations of the parenchymatous organs and bone marrow.

Case 18.—Major (1918) reports a case of a patient 42 years old who one month before admission developed headaches and malaise. Physical examination showed enlarged tonsils, enlarged spleen, and leukæmic blood. Duration two months. Autopsy showed a tumor of the anterior mediastinum, general glandular enlargement, and infiltration of the parenchymatous organs.

Case 19.—Weber (1919) reports a case of a patient 18 years old who one month before admission developed pains in the side. Physical examination showed a general glandular enlargement, large liver and spleen, fever, and leukæmic blood. X-ray treatment was followed by severe hemorrhages and death. Duration two and a half months. Autopsy showed a tumor of the anterior mediastinum, general glandular enlargement, infiltration of the parenchymatous organs and bone marrow. "Cells . . . . were probably large lymphocytes, but since a few gave a positive oxydase, I now think them to have been myeloblasts."

Case 20.—Weber (1919) reports a case of a patient seven years old who five months before admission developed malaise, pallor, and abdominal symptoms. Physical examination showed a general glandular enlargement, enlargement of liver and spleen, fever, and numerous hemorrhages. W. B. C. 103,125; P. M. N. 5.6%; myelocytes 4%, myeloblasts 94%. No P. M. E., no T. "Amongst the transitional forms . . . . probably some

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were lymphocytes. It was impossible to differentiate lymphocytes from the cells counted as myeloblasts. Blood films not satisfactory." Duration five and a half months. Autopsy showed a tumor of the mediastinum, general glandular enlargement, and infiltration of the parenchymatous organs.

CASE 21.—Harrison (1920) reports a case of a patient 29 years old who two months before admission developed epigastric symptoms. Physical examination showed dulness over the mediastinum. Blood was leukæmic. Duration four months. Autopsy showed tumor of the mediastinum, general glandular enlargement, and infiltration of the parenchymatous organs and bone marrow.

CASE 22.—Martin (1901) reports a case of a patient 45 years old who several years before admission developed enlarged cervical and inguinal lymph glands after an accident. Asthenia and anæmia progressed. Physical examination showed general glandular enlargement and large spleen and liver. Blood showed an increase in large lymphocytes. Death several years after onset. Autopsy showed tumor villi and papillæ on peritoneal and pleural surfaces. A general glandular enlargement and infiltration of the parenchymatous organs was also present.

CASE 23.—Warthin (1904) reports a case of a patient 30 years old who one month before admission developed abdominal symptoms. Physical examination showed an abdominal mass and leukæmic blood. Duration one and a half months. Autopsy showed enlargement of all the deep glands, tumor of the ileum, infiltration of parenchymatous organs and bone marrow.

CASE 24.—Sternberg (1915) reports a case of a patient 11 years old who five months before admittance developed respiratory symptoms. Physical examination showed leukæmic blood, hemorrhagic tendency, and remittent fever. Duration eight months. Autopsy showed tumor-like deposits in the dura, general glandular enlargement becoming confluent, and infiltration of parenchymatous organs.

CASE 25.—Sternberg (1915) reports a case of a patient 16 years old who seven weeks before admission developed swelling of the cervical glands. Blood examination showed an increase in number of W. B. C. Duration seven weeks. Autopsy showed general glandular enlargement tending to become confluent, infiltration of parenchymatous organs, tumor masses in both breasts.

CASE 26.—Sternberg (1915) reports a case of a patient ten years old who three months before admission developed tumor nodules on the skull. Blood examination showed leukæmia. Duration five months. Autopsy showed tumor in skull over parietal bone, infiltration of parenchymatous organs, some general glandular enlargement and enlarged tonsils.

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From these 26 cases the following observations are worthy of notice. (1) In 24 cases (92 per cent) the disease occurred in young individuals between the ages of 7 and 30 years. (2) Loss of weight, malaise, chest symptoms, and glandular swelling are prominent symptoms.

CHART NO. 1

Case.	Age.	Dur. of sympt.	Symptoms.	Physical exam.			Autopsy findings.				
				G. G. E.	Spl. Liv.	Blood.	Dur. dis.	G. G. E.	Paren. org.	Bone marr.	Tumor.
1	23	4 m.	Cerv. glds.....	+	+	+	7.5 m.	+	+	+	Med.
2	7	4 m.	Chest sympt....	+	+	+	7 m.	+	+	+	Med.
3	28	4 m.	Chest sympt....	+	+	+	6 m.	+	+	+	Med.
4	12	6 m.	Glands.....	+	+	+	7 m.	+	+	+	Med.
5	12	5 wk.	Œdema.....	+	+	+	2.5 m.	+	+	?	Med.
6	31	4 wk.	Spleen and liver.	?	+	+	6 m.	Lumbar	+		Med.
7	25	3 m.	G. G. E.....	+	+	+	5 m.	+	+	+	Med.
8	7	?	Cerv. glds.....	?	+	+	?	Cerv.	+		Med.
9	15	3 m.	Pains.....	+	+	+	4 m.	+	+		Med.
10	6 m.	4 m.	Tumors head...			+	5 m.	?	+		Med.
11	23	3 m.	Chest sympt....			+	3.5 m.	+	+		Med.
12	18	3 m.	Chest sympt....	+	+	+	5 m.	+	+		Med.
13	11	2 m.	Cerv. glds.....	+	+	+	4 m.	+	+		Med.
14	19	1 m.	Malaise.....	+	+	+	1.5 m.	+	+	+	Med.
15	24	4 m.	Chest sympt....			+	5 m.	+	+		Med.
16	19	3 wk.	Chest sympt....			+	?	+	+	+	Med.
17	16	3 wk.	Chest sympt....			+	4 m.	+	+	+	Med.
18	42	1 m.	Malaise.....	+	+	+	2 m.	+	+		Med.
19	18	1 m.	Pains.....	+	+	+	2.5 m.	+	+	+	Med.
20	7	5 m.	Abd. Malaise...	+	+	+	5.5 m.	+	+		Med.
21	29	2 m.	Abd. sympt.....			+	4 m.	+	+	+	Med.
22	45	?	Malaise. Glds.	+	+	+	?	+	+		Ser.
23	30	1 m.	Abd. sympt.....			+	1.5 m.	Deep	+	+	Ileum
24	11	5 m.	Chest sympt....			+	8 m.	+	+		Dura
25	10	3 m.	Tumor head....			+	5 m.	+	+		Skull
26	16	7 wk.	Cerv. glds.....			+	2 m.	+	+		Brsts.

NOTE.—G. G. E. = General glandular enlargement.
Spl. = Spleen.
Liv. = Liver.
Dur. Dis. = Duration of disease.
Paren. Org. = Parenchymatous Organs.
Bone Marr. = Bone Marrow.
Med. = Mediastinum.
Ser. = Serous surfaces.
Brsts. = Breasts.

(3) Leukæmic blood (lymphoid), large liver and spleen, general glandular enlargement with a tumor mass in the mediastinum or elsewhere may be looked for clinically. (4) The disease runs an acute course; 25 (96 per cent) of the 26 patients died within 1 year after the onset. (5) At autopsy, the findings are characteristic and may be

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summarized as follows; (a) general glandular enlargement (85+ per cent); (b) infiltration of parenchymatous organs (100 per cent) and bone marrow; (c) an invasive mediastinal tumor spreading more or less to pleura, diaphragm, and pericardium, (84 per cent) 21 cases; (d) microscopically, uniform extensive infiltration of lymphoid cells, measuring 5-6μ in diameter, with little cytoplasm, and nucleus containing coarse chromatin granules. Mitotic figures may or may not be conspicuous.

Lymphosarcoma

If one were to include under this term only cases coinciding with Kundrat's definition of lymphosarcoma, the group would be small indeed. Therefore, it seems wiser to consider all cases of lymphoid tumor or general lymphoid hyperplasia not accompanied by leukæmia. From this point of view 11 cases have been chosen from the autopsy records of The Johns Hopkins Hospital.

Abdominal Group

In this series the pathological findings are quite similar. Pitt, in 1899, briefly describing 18 cases, divides them according to origin; (1) tumors of the ileum and cæcum forming in the mucosa and submucosa, (2) tumors starting in the mesenteric glands forming a diffuse sheath beneath the intestinal serosa. MacCallum (1907) has described many of the following cases and regards the abdominal group as distinctive in that the predominating lymphoid cell is larger and more vesicular than that seen in the chest group.

Case 27.—Margaret G., white, female, age 24. Family and past history negative except for typhoid fever at 14 and occasional attacks of leucorrhœa. Present illness began one year ago with symptoms of indigestion. Vomiting began three weeks before admission. Loss of weight and sharp pains in the epigastrium, œdema of arms and legs, constituted the most recent symptoms. Examination in the hospital, April 18, 1890, showed a hard mass in the lower abdomen, irregular in outline. The right arm was extremely œdematous from shoulder to wrist. Exploratory laparotomy April 29 showed numerous intestinal adhesions and a mass which seemed to be related to the intestine. Temperature varied from 100° to 102°. Patient died May 8, 1890.

Autopsy 92. *Anatomical Diagnosis.*—Lymphosarcoma of mesenteric glands and intestine; volvulus of jejunum with ulceration into cavity of tumor; general anæmia, etc.

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Body: Medium sized. Extreme emaciation and anæmia. Abdomen distended with a large mass easily palpable. 800 c. c. of yellowish fluid are seen in the peritoneal cavity, evidence of fibrinous peritonitis about the spleen and in the pelvis. In the midline behind the greatly distended portion of the transverse colon appears a fluctuating tumor mass into which the small intestine seems to enter. *Heart* and *lungs:* Normal. *Kidneys:* Normal. *Liver* weighs 2500 grams, is large and pale. *Tumor:* Transverse and descending colon are adherent to a large tumor mass. The upper portion of the jejunum becomes greatly dilated as it passes into the tumor. At this point the lumen opens into a large cavity in the interior of the tumor which contains yellow fluid material. The intestine at this point is enormously dilated, its walls are thickened and covered with nodular masses. Farther down is another dilatation of the intestine which opens into a similar cavity. The remainder of the gut is normal.

Microscopic Pathology.—Intestinal tumor: Sections show a mass of lymphoid cells infiltrating diffusely the intestinal coats and forming solid aggregations. There is great regularity in the arrangement, size, and shape of these cells. They average 8μ in diameter, are usually circular, and are composed of a small amount of cytoplasm surrounding a deep-staining, rather irregularly shaped nucleus. Mitotic figures are infrequent. Stroma is delicate; blood vessels are numerous.

Briefly, a 24-year old woman comes to the hospital complaining of abdominal symptoms, vomiting and loss of weight, which has been noticed for one year. Physical examination, April 18, 1890, showed an abdominal tumor. The patient died about one year after onset. At autopsy a large tumor of the small intestine was discovered accompanied by an enlargement of the mesenteric and retroperitoneal glands. The liver was also enlarged. Microscopically, the tumor cells are large and regular, lymphoid in type. This case may be called an intestinal lymphosarcoma spreading to mesenteric and retroperitoneal glands with probable infiltration of the liver.

Case 28.—Peter S., white, male, age 27. Family and past history are negative. Four months before admission the patient developed an attack of diarrhœa, vomiting and painful micturition. No epigastric pains. Constipation for five days before admission. Examination, August 12, 1891, showed anæmia, emaciation, subnormal temperature, and a retracted abdomen tender on pressure. No tumor palpable. Spleen and liver not palpable. The patient died August 17, after a week of continual vomiting and passage of dark fluid stools.

Autopsy 225. *Anatomical Diagnosis.*—Multiple lymphosarcomata of small intestine, with secondary nodule in liver and infiltration of kidneys; fatty degeneration of heart muscle and liver; pneumonia; general anæmia and cachexia.

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Body: Shows extreme emaciation and anæmia. *Heart:* Normal. *Lungs:* Show early pneumonic patches in right lower lobe. *Spleen:* 100 grams. Normal. *Adrenals:* Normal. *Kidneys:* 255 grams each. They are mottled and pale, coarse striæ alternating with pale white patches. Other wedge-shaped yellow areas are seen in the cortex. *Liver:* Weighs 1580 grams. It is reddish-gray in color, soft in consistency and shows a small nodule in the right lobe.

Intestine: The large intestine is normal. The appendix measures 8 cm. in length, is thickened and fibrosed with lumen obliterated. In the small intestine, 265 cm. above the ileocæcal valve, is a constriction formed by a new growth in the wall corresponding to the mesenteric attachment. This growth measures 2 cm. in length. It is firm in consistency and extends for a short distance into the mesentery. 27 cm. higher up is another smaller, similar, growth, also situated at the mesenteric attachment. It apparently involves the mucous and submucous coats. Further up in the intestine are two other growths similar to the ones described. *Lymph glands:* Mesenteric, retroperitoneal, and all superficial glands as far as they can be examined, are normal. There are no traces of any metastases from the intestinal tumors except the one in the liver. *Other organs:* Normal.

Microscopic Pathology.—Tumor: Sections show a diffuse infiltration of large lymphoid cells separating muscle and connective tissue fibres, as well as invading the deeper portion of the mucosa. The cells are irregular in size (6-10μ) and shape. Nuclei are deeply staining. Very little cytoplasm is evident. The walls of the appendix are invaded by these cells. *Liver:* There is extensive periportal infiltration of lymphoid cells somewhat more irregular but otherwise quite similar to those described above. *Kidneys:* Throughout the cortex are collections of lymphoid cells surrounding glomeruli and tubules and often forming small nodules. They are quite irregular.

Briefly, a white man aged 27 years came to the hospital with abdominal symptoms of four months' duration. Physical examination August 12, 1891, showed a tender abdomen, enlarged liver and spleen, and emaciation. The patient died one week after admission; duration four and one-half months. Autopsy revealed multiple tumors of the small intestine with infiltration of liver and kidneys. The cells are large (6-7μ), regular, lymphoid in type. This case may, therefore, be grouped with intestinal lymphosarcomata accompanied by infiltration of liver and kidneys.

CASE 29.—Ray S., white, male, age 7. Family and past history are negative. Onset of present illness six months before admission with enlargement of cervical lymph glands. About one week later the patient contracted measles. He apparently had a mild attack and seemed perfectly well afterwards. During this time, however, the glands continued to increase in size, but caused no pain. About two weeks before admission

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the mother noticed nodules in the child's abdomen. One week before admission became nauseated and vomited considerably. Since then he has lost about 15 pounds. Physical examination January 18, 1905, showed an emaciated child with enlarged cervical glands, palpable axillary and inguinal glands, and numerous projecting immovable nodules in the abdomen. Liver and spleen are not felt. Blood examination showed slight secondary anæmia. Tonsils are much enlarged. An enlarged lymph node removed from the right groin was diagnosed as lymphosarcoma. January 23, 1905, the patient was discharged and five months later died at home.

Autopsy 2543. *Anatomical Diagnosis.*—Lymphosarcoma involving the pancreas, adrenals, spleen, lymph glands, stomach and intestine.

Body: Only the abdominal organs were sent for examination. The liver is not present. From the anterior edge of the stomach along the lesser curvature hang large rounded masses of homogeneous pearly gray tissue which lie at the root of the mesentery. Mesenteric glands are separately enlarged into round masses. The spleen is not enlarged, but shows numerous nodules scattered throughout its substance, quite unlike the Malpighian bodies. *Kidneys:* The ureter of the right kidney at a short distance from the pelvis of the kidney passes into a tumor mass and seems to have lost its lumen. *Adrenals:* Both are invaded by the tumor. *Aorta:* Is deeply embedded in a mass of enlarged lymph glands. *Mesenteric glands:* Are all involved. *Pancreas:* Is practically replaced by the tumor. *Intestines:* Are closely bound to the stomach by numerous nodules and dense adhesions. As one passes up the large intestine, scattered areas of thickening are encountered. These involve the transverse folds which stand out rigidly. In the cæcum nearly all of the folds have this appearance. The ileocæcal valve is thickened into a stout ring. The Peyer's patches above the ileocæcal valve are enlarged and form projecting masses. On passing up into the ileum, numerous rigid and thickened patches are encountered, with no ulceration. The walls of the duodenum are thickened so that its folds are enormously increased in bulk.

Microscopic Pathology.—Intestinal tumor: Sections show large lymphoid cells forming solid nodules and infiltrating diffusely the coats of the intestine separating the muscle and connective tissue fibres and scattered densely in the deeper part of the mucosa. These cells average 8μ in diameter, show little cytoplasm, and large vesicular nuclei with coarse chromatin particles. The extreme irregularity in the nuclei would indicate an amœboid activity during life. Mitotic figures are frequent. *Gland:* The capsule is infiltrated, sinuses and germinal centres are rendered inconspicuous by the dense and homogeneous invasion of the lymphoid cells described above. *Adrenal* and *spleen:* Show great accumulations of these cells. *Kidney:* Negative.

Briefly, a white child seven years of age came to the hospital with a six months' history of swollen lymph glands and nodules in the abdomen. Physical examination January 18, 1905, showed a general glandular enlargement, large tonsils, abdominal tumors and a normal

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W. B. C. count. The child died about one year after onset. At autopsy multiple tumors of stomach and intestine are noted, most evident in the duodenum and small intestine. There is a general glandular enlargement, and infiltration of the pancreas, spleen and adrenals. Microscopically, the cells are quite similar to the other cases. This case, then, may be considered as an example of intestinal lymphosarcoma, with infiltration of the parenchymatous organs and a general glandular enlargement.

CASE 30.—Edward W., white, male, age 57. Family and past history are negative. Onset of present illness about one year ago with tired feeling, and about one month ago, fever, chill and prostration. Since then the history has been one of progressive weakness, anorexia, and prostration, occasional night sweats and loss of weight. Physical examination January 2, 1905, showed loss of weight and palpable axillary glands, but no definite signs in chest or abdomen. The blood showed a secondary anæmia with an eosinophilia of 18%. Two months later numerous motile amœbæ were found in the stools. Eosinophilia had dropped to 6%. Shortly after, the patient had three large intestinal hemorrhages and died with signs of anæmia.

Autopsy 2496. *Anatomical Diagnosis.*—Multiple lymphosarcomata of intestine; nodules in the pancreas and adrenals; adhesive pericarditis; chronic pleural adhesions; hemorrhage into the intestine (amœbæ found in intestinal contents during life).

Body: Is that of a slenderly built middle-aged white man; the chest and abdomen show no changes on superficial examination. *Heart:* Adhesive pericarditis. *Lungs:* Show old pleural adhesions. *Spleen:* Is enlarged. On section the pulp is grayish red and soft; the Malpighian bodies are easily visible. *Liver:* Is not enlarged. Its surface is smooth. *Stomach, pancreas, adrenals* and *kidneys:* Stomach is normal except where it is bound to the pancreas. In the duodenum, opposite the head of the pancreas, the intestinal wall is greatly thickened. Directly behind this area are numerous and large lymph glands, homogeneous and pearly white. The tail of the pancreas is converted into a tumor mass. The left adrenal is surrounded by this tumor. Kidneys seem normal. *Retroperitoneal glands:* Are somewhat enlarged. *Intestines:* Are filled with fresh blood to a high point in the ileum. Lymphoid nodules are not especially prominent. There are no ulcerations in the colon. The Peyer's patches appear normal until a point is reached about 30 cm. above the ileocæcal valve where the folds become thickened, rigid, and firm. In this region the mucosa is deeply ulcerated, ragged and necrotic on the surface. The adjacent mesentery contains an enlarged lymph gland which on section is homogeneous and pearly white in color. Progressing up the ileum are irregular thickenings involving particularly the submucosa and muscularis. So on up the intestine these irregular patches of thickening are repeated

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until a point is reached about 100 cm. below the duodenum where six intestinal loops are extremely rigid due to a thickening in all the walls with no ulceration. The mesentery shows large, homogeneous, pearly white glands. *Inguinal glands:* Are not conspicuously enlarged.

Microscopic Pathology.—Intestine: Is extensively infiltrated by regular lymphoid cells averaging 8μ in diameter, composed of a small amount of cytoplasm and a large vesicular nucleus. *Lymph gland:* Sections show a homogeneous mass of lymphoid cells. The capsule is somewhat infiltrated, germinal centres are obliterated, sinuses are indistinct. The cells are similar to those described above. *Spleen, liver* and *kidneys:* Show no infiltration. *Pancreas, testicle, adrenal* and *bone marrow:* Show extensive infiltrations of lymphoid cells

Briefly, a white man, 57 years old, came to the hospital with a year's history of weakness, anorexia and loss of weight. Physical examination, January 2, 1905, showed loss of weight, an eosinophilia of 18 per cent, and motile amœbæ in the stools. After several large intestinal hemorrhages the patient died. Total duration, one year and one month. Autopsy showed multiple tumors of the small intestine, involvement of neighboring glands, and infiltration of the pancreas, adrenals, testicles and bone marrow. This, then, is a lymphosarcoma of the intestine which has extended to distant organs and to the bone marrow.

Case 31.—Emory H., white, male, age 17. Family and past history are negative. Three months before admission began to have pain in the abdomen on the left side, constantly present but worse after meals. He became constipated. Abdomen enlarged and a lump appeared in the hypochondrium. No nausea or vomiting. Weakness, dyspnœa, and pain increased. On examination, January 5, 1902, the abdomen appeared distended with numerous nodular masses. Blood count practically normal. Patient died three days after admission.

Autopsy 1842. *Anatomical Diagnosis.*—Persistent thymus; lymphosarcoma of the intestine with dilatation and ulceration of the ileum; metastases in the mesenteric, abdominal and retroperitoneal lymph glands involving the pancreas and right adrenal; metastases to liver, spleen, thymus, kidneys and bone marrow.

Body: Is somewhat emaciated with slight enlargement of axillary and inguinal glands. In the peritoneal cavity are three large tumor masses above and to the right of the bladder. The mesentery is thickened and filled with nodules. Enlarged lymph glands are found near the cardiac orifice, at the pylorus, and along the aorta. Both pleural cavities contain large amounts of yellow fluid. The thymus is much enlarged, measuring 11 x 4½ cm. Several large lymph glands, 8 x 5 cm. in diameter, are found in the mediastinum, also large nodular masses are noticed on the diaphragm. *Heart* and *lungs:* Normal. *Spleen:* Weighs 200 grams and shows

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nothing unusual. *Liver:* Weighs 1500 grams. Beneath the capsule and over the cut surface oval, white nodules, irregular in size, are distributed. *Kidneys:* Weigh 125 grams each and show several yellowish nodules. *Adrenals:* Are normal except the right adrenal is apparently embedded in the tumor mass below the liver. *Intestines:* The small intestine shows throughout its length numerous small, flat nodules situated beneath its membrane. The Peyer's patches are somewhat swollen. 45 cm. from the pylorus the jejunum disappears into a large tumor mass, the size of an infant's head. On opening the remainder of the ileum, down to the ileocæcal valve, a wonderful picture is disclosed. Three tumor masses are seen consisting of dilated portions of the ileum infiltrated with new growth and continuous with tumor nodules in the mesentery. The walls of the intestine are much thickened, in some places measuring over 3 cm. Large nodules, external to the ileum, are evidently coalesced mesenteric glands. The appendix and its mesentery are thickened and infiltrated with new growth. The large intestine is normal. Behind the rectum large masses of glands form nodules 4-5 cm. in diameter. These tumors have infiltrated the surrounding tissue, binding the rectum and pelvic fascia into one solid mass. Inguinal and iliac lymph nodes are enlarged.

Microscopic Pathology.—Intestinal tumor: Sections show large lymphoid cells in solid masses or infiltrating diffusely the intestinal coats, separating muscle fibres, connective tissue cells, and spreading out uniformly in the deep layer of the mucosa. Sections of the mucosa show little stroma and few blood vessels. The cells, uniformly placed, regular in size (8μ) and shape, show little cytoplasm and a large vesicular nucleus with occasional coarse, chromatin granules. Mitotic figures are numerous. *Lymph gland:* Here the cells are more irregular. They form the lymph cords displacing entirely germinal centers and normal lymphocytes. Sinuses contain only a few wandering cells and giant cells. *Spleen:* Large lymphoid cells form the Malpighian bodies and appear scattered through the pulp. *Liver* and *kidney, pancreas, adrenal, tonsil:* Are all extensively infiltrated with large lymphoid cells. *Thymus:* The usual architecture is obliterated by a homogeneous mass of lymphoid cells. *Bone marrow:* The hemopoietic cells are obscured by the homogeneous lymphoid infiltration.

Briefly, a white boy, 17 years of age, came to the hospital with a three months' history of abdominal pain and increasing weakness. Physical examination disclosed masses in the epigastrium and normal blood count. The patient died about three months after onset of symptoms. The autopsy showed multiple tumors of the small intestine with infiltration of parenchymatous organs, tonsils and bone marrow, general glandular enlargement, and a few nodules on the diaphragm. The cells are all of large lymphoid type, averaging 8μ in diameter. This case is an example of lymphosarcoma with general distribution throughout the body.

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CASE 32.—William F., black, male, age 55. Family and past history unimportant. Onset of present illness four months before admission with weakness, and abdominal pain. Physical examination, October 14, 1913, showed extreme emaciation and anæmia, a slight general glandular enlargement, and a mass in the epigastrium. The examination of the blood was incomplete but showed a slight leucocytosis and slight eosinophilia. The patient died the day after admission.

Autopsy 4010. *Anatomical Diagnosis.*—Lymphosarcoma of abdomen forming a sheath for the aorta and a capsule for kidney and pancreas, involving mesenteric and retroperitoneal glands, extending into the diaphragm, over the pleural surfaces, involving left adrenal; general anæmia and emaciation, etc.

Body: Is that of an emaciated colored man. Peritoneal surfaces are smooth. Beneath the omentum a huge mass extends from the dome of the diaphragm on the left side as far down as the pelvis, compressing the spleen, pushing the duodenum anteriorly, hiding all evidence of pancreas, left adrenal and left kidney. *Heart:* Negative. *Lungs:* Show areas of broncho-pneumonia. *Spleen:* Weighs 140 grams and appears normal. *Liver:* Weighs 1500 grams. Periportal areas are translucent and gray. *Kidneys:* The right kidney and adrenal seem normal. The left kidney is shelled out of a capsule of tumor tissue. On section it is enlarged and shows areas of infiltration. The ureter on this side is surrounded by tumor tissue which surrounds also the abdominal aorta. The adrenal is buried in this mass and seems almost destroyed. *Pancreas:* At its head seems normal. Elsewhere it is completely surrounded by an envelope of tumor. *Pelvic organs:* Normal. *Tumor:* Seems to consist, then, of enlarged mesenteric and retroperitoneal glands with extensive regional infiltration. *Gastro-intestinal tract:* Normal.

Microscopic Pathology.—Tumor: Sections through the retroperitoneal glands show solid masses of large lymphoid cells averaging 8μ in diameter, irregular in outline, with large irregular vesicular nuclei. Mitoses are frequent. Many of these cells contain two or three nuclei. *Spleen:* Possibly a few of these large cells are scattered about in the region of the Malpighian bodies. *Pancreas:* Extensively infiltrated. *Liver* and *kidney:* Negative.

Briefly, the patient, a colored man 55 years old, came to the hospital October 14, 1913, with a four months' history of abdominal pain. Physical examination disclosed a general glandular enlargement, masses in the epigastrium and a slight leucocytosis. Exitus four months after onset. At autopsy, tumors of the mesenteric and retroperitoneal glands were found extending to form a capsule about the kidney, involving pancreas, adrenal, diaphragm and pleura. There was a general glandular enlargement. The cells, except for evidence of amœboid activity, are quite similar to those seen in other cases. This case,

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occurring in an older individual, is of considerable interest. The process did not localize in the intestine but started in the mesenteric and retroperitoneal glands, spreading from there to pancreas, adrenal and other lymph glands.

CHART NO. 2.—SUMMARY OF ABDOMINAL GROUP

Case.	Age.	Dur.	Tumor.	Mes. Ret. Glands.	Liver.	Kid.	Panc. Adr.	Paren. organs.	G.G.E.	Bone marr.
27	24	1 y.	Sm. Int.	+	+	0	0	0	0	0
28	27	4.5 m.	Sm. Int.	0	+	+	0	0	0	?
29	7	1 y.	Sm. Int.	+	+	+	0	+	+	?
30	57	1 y.	Sm. Int.	+	0	0	+	0	?	+
31	17	3 m.	Sm. Int.	+	+	+	0	+	+	+
32	55	4 m.	Glands	+	0	0	+	0	+	?

Although no accurate conclusions may be drawn from the study of six cases, several interesting points should be mentioned. (1) The disease tends to occur in young individuals. (2) The disease runs a rapid course, usually within one year. (3) Abdominal discomfort, loss of weight, and malaise, are characteristic symptoms and abdominal tumor masses may be noted clinically. (4) At autopsy the findings are surprisingly similar. Single or multiple tumors of the small intestine (5 cases) or mesenteric glands (1 case) are encountered. These tumors spread locally to infiltrate retroperitoneal tissues, glands, adrenals, pancreas, etc. But further extension to spleen, liver and kidneys, lymph glands, deep and superficial, testicles and bone marrow, which occurs so characteristically, must take place by way of the blood stream.

MEDIASTINAL GROUP

Another point of predilection for this tumor formation seems to be in the glands of the mediastinum. Four cases from The Johns Hopkins Hospital pathological records will be described:

Case 33.—Hester B., black, female, age 60. Patient was admitted to the hospital August 10, 1899. No history was obtainable. Physical examination was unsatisfactory. The patient died the day after admission.

Autopsy 1402. *Anatomical Diagnosis.*—Tumor of mediastinum and heart; involvement of bronchial glands; acute pericarditis with adhesions; cardiac hypertrophy and dilatation; thrombus in right auricle; infarcts of spleen and kidney, etc.

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Body: Is that of a stout colored woman. Peritoneal cavity is normal. Chest cavities contain fluid. A tumor mass is seen in the anterior mediastinum at the base of the aorta, surrounding the trachea and involving pericardial lymph glands and bronchial glands. The tumor is white in appearance and on section is soft in consistency. *Heart:* The wall of the right ventricle is enormously enlarged and thickened by the tumor extension which almost entirely replaces the myocardium. *Lungs* and *lymph glands:* Negative. *Spleen:* Weighs 180 grams and shows infarcts. *Liver:* Appears mottled and cloudy. *Kidneys:* Are large and pale with distorted architecture. *Other organs:* Show no changes relative to our interest.

Microscopic Pathology.—The sections show a cellular tumor of the lymphoid type. The cells are irregular in size and shape, varying from 5-12μ in diameter, and range from spherical to spindle form. The nuclei are sometimes round, oval, sometimes budding, racquet shaped, and spindle shaped. The nucleus contains chromatin particles and except for differences in outline appears identical in each cell. Mitoses are frequent. The stroma is delicate. *Spleen, liver, kidneys* and *intestine:* Show no cellular infiltration.

Briefly, a black female, aged 60 years, was admitted to the hospital, August 10, 1899, practically moribund from some respiratory difficulty. No satisfactory history or physical examination was obtainable. Autopsy showed an invasive tumor of the mediastinum, involving pericardium and heart. No general glandular enlargement and no infiltration of the parenchymatous organs were present. The tumor cells are irregular in size (5-12μ) and shape, composed of pleomorphic nucleus and prominent cytoplasm. This case may be regarded, then, as a strictly localized lymphosarcoma of the mediastinum (Kundrat).

Case 34.—N. G., black, male, age 47. Family and past history are unimportant. Present illness began ten months before admission with a small nodule in the neck. Four months ago glands on both sides of his neck and above the clavicle were very large, his voice changed, and he began to have difficulty in swallowing and breathing. Physical examination December 22, 1917, showed signs of respiratory distress, tremendous enlargement of the cervical glands, and a moderate enlargement of all the superficial glands. Liver was palpable. Spleen not felt. X-ray showed a mediastinal mass. Examination of blood normal. The patient died two days after admission from respiratory difficulty. His temperature was subnormal until the last day.

Autopsy 5402. *Anatomical Diagnosis.*—Lymphosarcoma of cervical, axillary and mediastinal lymph glands; invasion of trachea and pleura; involvement of right vagus and both recurrent laryngeal nerves; œdema of glottis; tracheotomy wound; thrombosis of both subclavian and axillary veins; lobular pneumonia.

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Body: Is that of a well preserved, middle-aged, negro man. The neck is much enlarged due to the presence of nodular masses on the right and left sides, beneath the jaws and extending down to the clavicles. The inguinal glands are enlarged. Retroperitoneal and mesenteric lymph glands are of about normal size. *Heart:* Normal. *Lungs:* Show a few tumor metastases and early lobular pneumonia. Lymph nodes at the hilum are apparently uninvolved. *Spleen:* Weighs 185 grams and is apparently normal. *Liver:* Weighs 1680 grams and shows no changes in the gross. *Kidneys:* Normal. *Tumor:* Is composed of large whitish nodules, apparently lymph glands. In many areas they coalesce to form large conglomerate masses and in other places the tumor invades the tissues and is not confined to the glands. What is apparently the primary tumor forms a large conglomerate mass in the neck stretching from ear to ear, down beneath the clavicles to form a large mass in the mediastinum. It surrounds the nerves and trachea and extends over the pleura. Both axillary groups of glands form large confluent masses.

Microscopic Study.—The tissues have been poorly fixed so that careful study of the sections is very difficult. *Tumor:* Is of the lymphoid type; homogeneous and cellular. The cells are irregular in size (6μ) and shape, cytoplasm is indistinct. The nuclei are rather vesicular. *Mediastinal gland:* Seems infiltrated by lymphoid cells of the type described above. These cells obliterate germinal centers, fill and distort the sinuses, and replace all but a few lymphocytes which are pushed peripherally against the capsule. *Spleen, liver, kidney* and *bone marrow:* Show no invasion of lymphoid cells.

Briefly, a colored man, aged 47 years, came to the hospital with large cervical glands of 10 months' duration, which produced difficulty in breathing and swallowing. Physical examination December 22, 1917, showed a cervical tumor, palpable superficial glands and enlarged liver. X-ray disclosed a mediastinal mass. The blood examination was negative. The patient died two days after admission. Autopsy revealed an invasive tumor of the mediastinum, enlargement of all superficial glands but no infiltration of the parenchymatous organs. Everywhere the tumor cells were of the lymphoid type, irregular in size (6μ) and shape, but similar in general morphology. This case may be regarded, therefore, as a lymphosarcoma of the mediastinum with involvement of all superficial lymph glands.

CASE 35.—John K., white, male, age 27. Family and past history are negative. Present illness began six weeks before admission with cough, dyspnœa and swelling on the left side of the neck. Dysphagia developed shortly after. Physical examination August 27, 1889, showed enlarged cervical glands and tonsils, but no perceptible increase in size of axillary or inguinal glands. The patient died suddenly the day after admission.

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Autopsy 22. *Anatomical Diagnosis.*—Lymphosarcoma of mediastinal and cervical lymph glands, pericardium, myocardium, and pleura; chronic passive congestion of abdominal viscera.

Body: Is that of a well nourished young man, weighing about 175 pounds. Large masses are palpable on the left side of the neck. On removing the sternum a tumor irregular in outline with an average diameter of 17 cm. is seen. It occupies the mediastinum, extending into the right and left pleural cavities, over the pericardium, and around the great vessels. It involves all the mediastinal glands and is continuous with the glandular swellings in the neck. On section the tumor appears mottled, soft and moist, similar to the cervical glands. *Lungs:* Show an occasional tumor nodule, evidently a direct extension. The bronchial glands appear similar to the tumor mass. *Tonsils:* Are very large and of the same color and consistency as the tumor. *Heart:* Normal except for thick masses on the epicardium surface opposite the tumor in the pericardium. *Diaphragm:* Is covered with small nodules. *Spleen:* Weighs 310 grams. On section a number of soft, whitish, nodules are seen. *Liver:* Weighs 2000 grams. On section it appears normal. *Pancreas, adrenals, kidneys:* Normal. *Lymph glands:* All the mesenteric and retroperitoneal glands are enlarged. In general they present the same appearance as the tumors. *Gastro-intestinal tract:* Normal, except for the enlargement of solitary follicles in the large intestine.

Microscopic Pathology.—The sections show a cellular tumor of the lymphoid type. The cells are quite regular in size (5-7μ) and shape. Usually little or no cytoplasm is visible. The nucleus is sharply outlined, uniform, containing coarse chromatin granules. Mitotic figures are numerous. Stroma is scanty. *Spleen:* Malpighian bodies are hypertrophied and show in their vicinity large lymphoid cells which are also scattered throughout the pulp. It is difficult to relate these cells with those concerned in the mediastinal tumor. *Liver:* Here, however, the periportal accumulations of lymphoid cells are definite. Between the connective tissue cells, wandering through the liver lobules, they often assume bizarre forms. Mitoses are frequent. *Kidney:* Sections show no lymphoid infiltration. *Intestine:* The mucosa and submucosa are distended by a very dense infiltration of lymphoid cells.

Briefly, a white man, aged 27 years, came to the hospital with a cervical tumor of six weeks' duration which was producing difficulty in breathing and swallowing. Physical examination, August 27, 1889, disclosed enlargement of the cervical glands and tonsils. No blood examination was recorded, for the patient died a few hours after admission. Autopsy showed an invasive tumor of the mediastinum, a general glandular enlargement with infiltration of intestine and liver. Everywhere the tumor cells were of the lymphoid type, regular, and similar in size (6μ), shape, and general morphology. Presuming the blood to

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have been normal, we may regard this case as a lymphosarcoma of the mediastinum accompanied by a general glandular enlargement and beginning infiltration of the parenchymatous organs.

CASE 36.—William O'K., white, male, age 57. Family and past history are negative. Present illness began four months before admission with cough, dyspnœa, and numerous attacks of hemoptysis. Physical examination, January 21, 1918, showed orthopnœa, cyanosis of face and neck, and a mass just above the clavicle extending over the right side of the neck. Retromanubrial dulness increased. Liver palpable. Wassermann negative. X-ray of chest showed a mediastinal mass. Diagnosis of excised lymph gland—lymphosarcoma. Examination of blood showed slight secondary anæmia. Radium treatment was administered for one month, but the patient continued a downward course and died March 6, 1918.

Autopsy 5467. *Anatomical Diagnosis.*—Lymphosarcoma of mediastinum invading right lung, superior vena cava and pericardium; metastases to adrenal and bone marrow; radiation of thorax; early degeneration of tumor cells; hemothorax and hemopericardium.

Body: Is that of a white man weighing 117 pounds. There is a large mass at the root of the neck just above the right clavicle. No glands are felt in the left side of neck, axilla or groin. Both pleural cavities are filled with bloody fluid. A large tumor mass occupies the mediastinum and invades extensively the upper right lung and parietal pleura. Tumor nodules stud the pleura and pericardium, invade the superior vena cava and left innominate vein, trachea, and right primary bronchus. Pericardial sac contains a small quantity of bloody fluid. *Heart:* Is normal except for tumor masses extending through the pericardium. *Spleen:* Weighs 125 grams and seems normal. *Liver:* Weighs 1810 grams and seems normal. *Intestines:* Show no hyperplasia of the lymphoid follicles. *Adrenals:* Are enlarged and pale. *Kidneys:* Seem normal. *Pelvic organs* and *Neck organs:* Normal.

Microscopic Pathology.—Tumor: Sections show a cellular tumor of the lymphoid type. The cells are observed in solid masses, equidistant. They are irregular in size (6-8μ) and shape. The nucleus is filled with coarse chromatin granules. Mitoses are frequent. *Spleen, liver* and *kidney:* Show no evidence of lymphoid infiltration. *Adrenal:* Nodules of lymphoid cells quite like a tumor metastasis are invading the adrenal cortex. *Bone marrow:* Solid masses of lymphoid cells replace entirely the hemopoietic tissue.

Briefly, a white man, aged 57 years, came to the hospital with a four months' history of cough, orthopnœa, and hematemesis. Physical examination January 21, 1918, showed cervical tumors, a palpable spleen, a mass in the mediastinum, and mild secondary anæmia. An excised gland was diagnosed lymphosarcoma. After numerous treatments by radium the patient died March 6, 1918, about six months

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after onset. The autopsy revealed an invasive tumor of the mediastinum with distant nodules in the adrenals and infiltration of the bone marrow. No general glandular enlargement and no infiltration of the parenchymatous organs was noted. Everywhere the cells were of lymphoid type, similar in size (6-8μ), shape and general morphology. This case might be classed with the lymphosarcomata of the mediastinum with extension by the blood stream to adrenal and bone marrow. marrow.

CHART NO. 3.—SUMMARY OF MEDIASTINAL GROUP

Case.	Age.	Duration.	Tumor.	G. G. E.	Parenchymatous organs.	Bone marrow.
33	60	?	Mediastinum	0	0	?
34	47	10 m.	Mediastinum	Superf.	0	0
35	27	6 wk.	Mediastinum	+	Liver and intestine	?
36	57	6 m.	Mediastinum	0	Adrenals	+

This group, also, is small for statistical study. Similarity to the abdominal group as regards mode of extension is striking. The tumor may be strictly localized (Case 33) or may spread progressively by way of the blood stream.

CLINICAL GROUP

From the clinical standpoint, the question of lymphosarcoma is even more confusing. Microscopic examination of an affected gland will rule out tuberculosis, secondary tumor, etc. But can the pathologist distinguish between Hodgkin's disease and lymphosarcoma, can he even diagnose these conditions, and, more important, can he give a reliable prognosis?

To answer these questions, the following cases, 26 lymph glands removed at operation, examined by different pathologists, and diagnosed lymphosarcoma, have been chosen.

Case 37.—W., white, male, age 53. S. P. 3100. Lumps in left axilla September, 1898 (20 months before admission). January, 1900, pain and rapid increase in size; May, 1900, size of child's head. Operation: excision of tumor and glands. Death one month later. Duration 21 months.

***Gland.*—Microscopic sections: Homogeneous mass of lymphoid cells. Capsule invaded, sinuses and germinal centers obliterated. Stroma increased. Predominating cell is of lymphoid type, averaging 8μ in diameter,**

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very amœboid. Nucleus is vesicular, and in many cells mitoses are seen. Nuclear fragments are abundant. There is some endothelial hyperplasia; few eosinophiles are seen; few normal lymphocytes.

CASE 38.—D., white, female, age 62. S. P. 3195. Tumor over left jaw two months. Rapid growth with pain. Examination showed swelling in right side of neck, 8 x 12 cm., and lumps over left jaw. Operation July 23, 1900, tissue for diagnosis. Death one month later. Duration three months.

Gland.—Microscopic section: Homogeneous mass of lymphoid cells. Capsule not invaded, sinuses and germinal centers obliterated. Stroma not increased. Predominating cell is of lymphoid type, averaging 8μ in diameter. No evidence of amœboid movement. Nucleus is vesicular; mitoses frequent. No other cells are conspicuous.

CASE 39.—V., white, male, age 52 years. S. P. 4245. Swelling at angle of jaw for 15 months. Rapid growth. Loss of weight. Glands appeared in neck, groin and axilla. Operation June, 1902; gland for diagnosis. Death one hour later. Duration 15 months.

Gland.—Microscopic section: Homogeneous lymphoid masses in cords and strands between delicate reticulum. Capsule not invaded; sinuses and germinal centers obliterated. Stroma not increased. Predominating cell is of lymphoid type, averaging 8μ in diameter. Amœboid movement marked. Nucleus vesicular with coarse chromatin. Frequent mitoses.

CASE 40.—P., white, female, age 2. S. P. 8400. Abdominal symptoms five months. Loss of weight. Operation, August 14, 1907, nodules attached to all viscera. No general glandular enlargement; lumen runs through tumor tissue.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells. Capsule not invaded, sinuses and germinal centers obliterated. Stroma not increased. Predominating cell is of lymphoid type, averaging 7μ in diameter. No evidence of amœboid activity. Nucleus is vesicular; chromatin coarse; numerous mitoses. No other cells.

CASE 41.—M., white, male. S. P. 10718. Masses in nasopharynx and enlarged glands two months. Operation, July, 1910; excision of glands. Death two months later. Duration four months.

Glands.—Microscopic note: Homogeneous mass of large lymphoid cells. Capsule not invaded, sinuses and germinal centers obliterated. No increase in stroma. Predominating cell is of lymphoid type, averaging 9μ in diameter. Amœboid activity marked. Nucleus vesicular with coarse chromatin. Many mitoses. Endothelial lined sinuses are evident. No eosinophiles; a few normal lymphocytes are crowded in small islands.

CASE 42.—S., white, male, age 63. S. P. 10996. Tumor at angle of jaw six months. Operation November 10, gland for diagnosis. Recurrence two years later. Death. Duration three years and eight months.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells. Capsule extensively invaded. Germinal centers obliterated; hyperplastic

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sinuses visible. No increase in stroma. Predominating cell is of lymphoid type, unusually regular, averaging 6-7μ in diameter. Nuclei somewhat vesicular; chromatin fine; no mitoses. No other cells.

CASE 43.—S., white, male, age 23. S. P. 12304. Lumps behind ear and in abdomen four weeks. Loss of weight. Operation December, 1911; excision of gland for diagnosis. Death two weeks later. Duration six weeks.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells. Capsule infiltrated. Germinal centers and sinuses obliterated. Stroma not increased. Predominating cell of lymphoid type, quite regular, averaging 7μ in diameter. Nuclei vesicular with coarse chromatin; mitoses frequent. Few larger endothelial cells.

CASE 44.—R., white, female. S. P. 13080. Tumors of scalp and cervical glands two years and three months. Operation, August, 1912; excision of gland for diagnosis followed by excision of glands. Patient lost trace of.

Gland.—Microscopic note: Mass of lymphocytes supported in an irregular reticulum. Capsule is invaded; germinal centers and sinuses are obliterated. Stroma is prominent. Predominating cell is of lymphoid type (8-10μ) in diameter, very amœboid. Nuclei are vesicular with coarse chromatin. Many mitoses are seen. Endothelial cells are scattered about.

CASE 45.—J., white, male, age 22. S. P. 14132. Cervical tumors six months. Later general glandular enlargement and difficulty in swallowing. Operation, January, 1913; excision of gland for diagnosis. Patient lost trace of.

Gland.—Microscopic note: Mass of lymphocytes, homogeneous, infiltrating capsule, obliterating germinal centers and sinuses. No increase in stroma. Predominating cell is of lymphoid type, 7-8μ in diameter, regular in size and shape. Nuclei are somewhat vesicular; chromatin rather coarse; no mitoses; many eosinophiles clumped and scattered.

CASE 46.—K., white, male, age 45. S. P. 14623. Lump beneath right ear eight months. Mass extended to clavicle. Operation September, 1913; excision of gland for diagnosis. Death one month later. Duration nine months.

Gland.—Microscopic note: Confused mass of lymphoid cells, invades capsule, surrounds hyperplastic germinal centers and fills sinuses. Stroma seems somewhat more prominent. Predominating cell is of lymphoid type, 6-7μ in diameter, regular in size and shape. No amœboid activity. Nuclei somewhat vesicular. Chromatin rather coarse; many mitoses. Few normal lymphocytes; moderate sprinkling of endothelial cells; many P. M. eosinophiles.

CASE 47.—P., white, male, age 55. S. P. 15855. Tumor of occiput six months. Operation, June, 1914; excision of mass. Later, after radium treatment, general glandular enlargement and a mass in the epigastrium developed. Death. Duration one year and four months.

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Gland.—Microscopic note: Mass of lymphoid cells surrounding hyperplastic germinal centers. Sinuses obliterated. Capsule infiltrated. Stroma not increased. Predominating cell is of lymphoid type, 6-7μ in diameter, regular in size and shape. Nuclei vesicular containing coarse chromatin. No mitoses. Few endothelial cells; few eosinophiles.

Case 48.—M., white, male, age 45. S. P. 16488. Infected antra three years; polyps two years. Recurred three months after operation. General glandular enlargement one year. Operation, November, 1914, pharyngeal tumor section for diagnosis. Patient lost trace of.

Gland Tumor.—Microscopic note: Homogeneous mass of lymphoid cells, infiltrating capsule, obliterating germinal centers and sinuses. No increase in stroma. Predominating cell is of lymphoid type, 8μ in diameter. Amœboid activity pronounced. Nuclei are vesicular and contain coarse chromatin granules. Mitoses are frequent. No other cells.

Case 49.—N. L. Operation December, 1914; glands of neck. Patient lost trace of.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells. Capsule infiltrated, germinal centers and sinuses obliterated. Slight increase in stroma. Predominating cell is of lymphoid type, 6-8μ in diameter. Some evidence of amœboid activity. Nuclei vesicular with coarse chromatin. Many mitotic figures; many eosinophiles; few endothelial cells.

Case 50.—B. S. P. 17083. Operation: excision of axillary glands. Patient lost trace of.

Gland.—Microscopic note: Homogeneous lymphoid mass. Capsule infiltrated. Germinal centers present but small; sinuses dilated and filled with cells. Stroma not increased. Predominating cell is of lymphoid type, 6-8μ in diameter, amœboid. Nuclei vesicular with coarse chromatin. Few mitoses. Many lymph spaces lined by endothelial cells.

Case 51.—S. S. P. 17606. Enlarged tonsils followed by enlarged glands of the groin. Patient lost trace of.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells. Capsule infiltrated, germinal centers not seen; sinuses dilated and filled with cells. No increase in stroma. Predominating cell is of lymphoid type, 6-7μ in diameter, showing evidence of amœboid activity. Nuclei coarse and vesicular, with distinct chromatin granules. No mitoses. Few endothelial cells.

Case 52.—O. S. P. 21219. Operation March, 1917; excision of glands of neck. Death two months later.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells involving the capsule and obliterating sinuses. Germinal centers barely distinguishable. Slight increase in stroma. The predominating cell is lymphoid in type. It is very amœboid, irregular in shape, about 8μ in diameter. The nucleus is vesicular with coarse chromatin granules. Frequent mitoses. Few endothelial and phagocytic cells.

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CASE 53.—P., white, male, age 21. S. P. 21883. Lumps on scalp three months. Difficulty in swallowing and enlargement of cervical glands one month. Examination showed a general glandular enlargement and a mediastinal tumor. W. B. C. 35,000, mostly polymorphs. Operation July, 1917; excision of gland for diagnosis. Death shortly after radium treatment. Duration three and a half months.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells invading capsule and obliterating sinuses and germinal centers. No increase in stroma. Predominating cell is of the lymphoid type, about 7-8μ in diameter, regular in size and shape. No sign of amœboid activity. Nuclei are vesicular with coarse chromatin. Numerous mitoses.

CASE 54.—S., white, female, age 35. Soreness in throat and fulness for some months. January, 1917, doctor diagnosed white spot as ulcer. No palpable glands. August, 1917, tonsilectomy with cautery. W. B. C. 7,600. L. and S. M. 37%. Note says "tonsil was not encapsulated, but resembled lymphosarcoma." December, 1917, after enlargement of glands, submaxillary and parotid and lymph glands were removed with external jugular vein. Tonsils diagnosed benign, but restudy and examination of glands removed showed lymphosarcoma of tonsil and glands. Radium treatment was given. No recurrence of right side, but left tonsil became involved and on January 26, 1919, patient died.

Metastases to top of head; cervical glands; glands on anterior chest and axilla. Severe sciatica last few months indicated lumbar metastases. Could not swallow water during last few days. Last month T. 102°. Last few weeks normal. Death one year and five months after first operation and one year and eleven months after first symptom.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells invading capsule and obliterating sinuses and germinal centers. No increase in stroma. Predominating cell is of lymphoid type, 9-10μ in diameter, quite regular. Nucleus is vesicular with coarse chromatin granules. Mitoses numerous. Eosinophiles present.

CASE 55.—B., white, male, age 42. S. P. 23687. General glandular enlargement; mass in groin. Operation September, 1918; excision of gland for diagnosis. Patient lost track of.

Gland.—Microscopic note: Mass of lymphoid cells surrounding hyperplastic germinal centers. Capsule invaded. Germinal centers hyperplastic and composed of large lymphoid cells similar to those described below. Sinuses are indistinct. Stroma is not increased. Predominating cell is of lymphoid type, 8μ in diameter. In places it is regular in shape, in other areas slightly amœboid. Nuclei are somewhat vesicular and hyperchromatic. Mitoses are frequent. No other cells seen.

CASE 56.—M., white, male, age 14. S. P. 23705. Enlarged cervical glands two months. Examination showed a general glandular enlargement and mass in abdomen. W. B. C. 4,500, with lymphocytes 36%. Operation Octo-

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ber, 1918; excision of gland for diagnosis. Death four months later. Duration six months.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells. No invasion of capsule. Sinuses and germinal centers obliterated. No increase in stroma. Predominating cell is lymphoid type, regular in size (7-8μ). There is no evidence of amœboid activity. Nuclei are vesicular with coarse chromatin granules. Many mitotic figures. No other cells.

Case 57.—C., white, male, age 56. S. P. 23727. Left tonsil enlarged two and a half years. Partial tonsilectomy. Enlarged glands of neck seven months. Operation October, 1918; excision of gland for diagnosis. Death three months later. Duration three years.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells closely packed and invading capsule, obliterating germinal centers and sinuses. No increase in stroma. Predominating cell of lymphoid type. Extreme amœboid activity. Cells average 8μ in diameter with vesicular nuclei containing coarse chromatin granules. Mitoses frequent. No other cells.

Case 58.—F. S. P. 23981. Operation, excision of glands for diagnosis. Patient dead. Duration eight + months.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells. Capsule not invaded. Germinal centers and sinuses are indistinct. No increase in stroma. Predominating cell is of lymphoid type. It measures 6-7μ in diameter; quite amœboid. Others are regular, still others are fragmented. Nuclei are large and somewhat vesicular with coarse chromatin particles. Many mitoses. Considerable hyperplasia of endothelial cells. Many phagocytic cells.

Case 59.—M., white, female, age 42. S. P. 9525. Lump in right axilla three months; soft, painful, freely movable. Nothing in either breast. Wassermann negative. Operation February, 1909; excision of gland. Patient living and well eleven years.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells. No definite invasion of capsule. Germinal centers and sinuses are very indistinct. No increase in stroma. Predominating cell of lymphoid type, 5-6μ in diameter, and regular. No amœboid activity. Not especially vesicular; no coarse chromatin. No mitoses. Some endothelial hyperplasia. Few wandering cells.

Case 60.—H., white, male, age 19. S. P. 19836. Skin rash and enlarged axillary glands three weeks. Small glands palpable in neck. W. B. C. 15,000; normal differential count. Wassermann negative. Operation July, 1916; gland removed for diagnosis. Treated with radium. Patient well four years.

Gland.—Microscopic note: No invasion of capsule. Masses of lymphoid cells surround the hyperplastic germinal centers. The germinal center cells are large and vesicular; they are surrounded by a ring of normal lymphocytes. The sinuses are filled with lymphoid cells. Predominating

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CHART NO. 4

Case.	Pt.	Clinical history.	Examination.	Operation.	Result.	Duration.	Lymph gland: microscopic study. Gen'l appearance.	Predominating lymphoid cell. Caps.	G. C.	Sin.	Str.	Size.	Am.	Nuc.	Chr.	Mit.	End.	L.	E.
37	W.M. 53	Left axilla 20 mos.....	Tumor left axilla 20 cm..	5-1900	Dead	21 m.	Hom. mass cells..	+	0	0	++	8μ	++	Ves.	+	+	+	+	+
38	W.F. 62	Left jaw 2 mos.....	Tumor right jaw 8x12 cm.	7-1900	Dead	2 m.	Hom. mass cells..	0	0	0	+	8μ	0	Ves.	+	+	0	0	0
39	W.M. 52	Left jaw 15 mos. G.G.E.	Tumor left jaw 29 cm.....	6-1902	Dead	15 m.	Cords and islands.	0	0	0	+	8μ	++	Ves.	+	+	+	0	0
40	W.F. 2	Abdomen 5 mos.....	Tumor abd. glds. ovary...	8-1907	Dead	5 m.	Hom. mass cells..	0	0	0	+	7μ	0	Ves.	+	+	+	0	0
41	W.M. ?	Tonsilitis large glds.....	Tumor nasopharynx.....	7-1910	Dead	4 m.	Hom. mass cells..	0	0	0	+	9μ	++	Ves.	+	+	+	0	0
42	W.M. 63	Left jaw 6 mos.....	.....	11-1910	Dead	3 y. 8 m.	Hom. mass cells..	++	0	+	+	7μ	0	Ves.	0	+	0	0	0
43	W.M. 23	Lump abd. and ear. 1 mo.....	Loss wt. 30 lbs.....	12-1911	Dead	6 wk.	Hom. mass cells..	+	0	0	+	7μ	0	Ves.	+	+	+	0	0
44	W.F. ?	Cerv. glds. 2 y. 3 mos.....	Tumors scalp.....	11-1912	?	?	Cords and islands.	+	0	0	++	8μ	++	Ves.	+	+	0	0	0
45	W.M. 22	G. G. E. 6 mos. dysphagia.....	.....	1-1913	?	?	Hom. mass cells..	+	0	0	+	7μ	0	Ves.	+	+	+	+	+
46	W.M. 45	Right ear 8 mos.....	Tumors cerv. glds.....	9-1913	Dead	9 m.	Cells surr. g. c...	+	+	+	+	7μ	0	Ves.	+	+	+	0	+
47	W.M. 55	Occiput 6 mos.....	.....	6-1914	Dead	1 y. 4 m.	Cells surr. g. c...	+	+	0	+	7μ	0	Ves.	+	+	+	0	0
48	W.M. 45	Nasal polyps 2 y.....	G. G. E. tumor nasoph....	11-1914	?	?	Hom. mass cells..	+	0	0	+	8μ	++	Ves.	+	+	+	0	0
49	W.M. ?	.....	Cerv. glands.....	12-1914	?	?	Hom. mass cells..	+	0	0	+	7μ	+	Ves.	+	+	+	0	0
50	.....	.....	Cerv. and axillary glds...	?	?	?	Hom. mass cells..	+	0	+	+	7μ	+	Ves.	+	+	+	0	0
51	.....	Enlarged tonsils.....	G. G. E.....	?	?	?	Hom. mass cells..	+	0	+	+	6μ	+	Ves.	+	+	+	0	0
52	.....	.....	Cerv. glands.....	3-1917	Dead	2 + m.	Hom. mass cells..	+	0	0	+	8μ	+	Ves.	+	+	+	0	0
53	W.M. 21	Scalp 3 mos.....	G. G. E. mediastinum.....	7-1917	Dead	3 m.	Hom. mass cells..	+	0	0	+	7μ	0	Ves.	+	+	+	0	0
54	W.F. 35	Tonsilitis 3 mos.....	Cerv. glands.....	12-1917	Dead	2 y.	Hom. mass cells..	+	0	0	+	9μ	0	Ves.	+	+	+	0	0
55	W.M. 42	Mass left groin.....	G. G. E.....	9-1918	?	?	Cells surr. g. c....	+	+	+	+	8μ	±	Ves.	+	+	+	0	0
56	W.M. 14	Cerv. glds. 2 mos.....	G.G.E. mass abd.....	10-1918	Dead	6 m.	Hom. mass cells..	0	0	0	+	7μ	0	Ves.	+	+	+	0	0
57	W.M. 56	Tonsils 2.5 y.....	Cerv. glands	10-1918	Dead	3 y. 6 m.	Hom. mass cells..	+	0	0	+	8μ	+	Ves.	+	+	0	0	0
58	.....	.....	.....	1-1919	Dead	8 + m.	Hom. mass cells..	0	0	0	+	6μ	+	Ves.	+	+	+	0	0
Summary																			
22	.....	.....	.....	.....	Probably dead	3 m.—4+y.	17 Homogeneous.. 77%.....	16 72%	17 77%	17 77%	2 18%	7μ	12 54%	22 100%	21 95%	18 80%	10 45%	4 18%	6 27%
59	W.F. 42	Right axilla 3 mos.....	Axillary gld.....	2-1919	Well	11 y.	Hom. mass cells..	0	0	0	+	6μ	0	Ves.	0	0	+	0	
60	W.M. 19	Rash, axillary glds. 3 wks....	Cerv. and axill. glds.....	7-1916	Well	4 y.	Cells surr. g. c....	0	++	+	+	8μ	0	Ves.	+	+	+	+	
61	W.M. 44	Groin.....	G.G.E.....	5-1917	Well	3 + y.	Gld. morph. dist..	+	++	+	+	7μ	0	0	0	0	+	+	
62	W.M. 53	Cerv. glds. 6 mos.....	G.G.E.....	2-1919	Well	2 y.	Hom. mass cells..	+	0	0	+	8μ	0	0	0	+	0		
Summary																			
4	.....	.....	.....	.....	Living	2 y.—11 y.	2 Homogeneous...	2	2	2	....	7μ	0	2	1	2	2	2	0

NOTE.—Caps.= Capsule.
G. C.= Germinal centers.
Sin.= Sinuses.
Str.= Stroma.

Am.= Evidence of amœboid activity.
Nuc.= Nucleus.
Ves.= Vesicular.
Chr.= Chromatin coarse.

Mit.= Mitoses.
End.= Endothelial cells.
L.= Normal Lymphocytes.
E.= Eosinophiles.

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cell is of lymphoid type about 8μ in diameter and quite regular. Nucleus is vesicular, chromatin coarse. Many mitoses.

CASE 61.—H., white male, age 44. S. P. 21470. Lumps in groin. All superficial glands palpable. Blood count normal. Operation May, 1917; gland removed for diagnosis. Well three years.

Gland.—Microscopic note: The gland morphology is distinct. Capsule slightly infiltrated. Germinal centers hyperplastic, filled with large central cells surrounded by a ring of lymphocytes. Sinuses can be determined. Large areas of necrosis with pycnotic nuclei are seen. Predominating cell is of lymphoid type. They measure 6-8μ in diameter; show no signs of amœboid activity. Nuclei are not vesicular; no coarse chromatin; no mitoses. Few larger cells with vesicular nuclei. Some endothelial cell hyperplasia.

CASE 62.—C., white, male, age 53. S. P. 24104. Family history of tuberculosis. Primary syphilitic lesion. Mass on left side of neck six months. Examination showed besides this palpable inguinal glands. Wassermann negative. Operation February, 1919; gland removed for diagnosis. Patient well one and a half years.

Gland.—Microscopic note: Homogeneous mass of lymphoid cells infiltrating capsule, obliterating germinal centers and sinuses. No increase in stroma. Predominating cell is of lymphoid type averaging about 8μ in diameter. No amœboid activity. Nuclei are pale and round; no coarse chromatin particles. Numerous mitoses. No other cells.

Fifteen cases are dead; seven cases, although no report has been received, were so far advanced that they may safely be classed with the fatalities, bringing the total to 22 cases. Four cases are living, one after 11 years, one after 4 years, one after 3 years and one after 2 years.

All ages are affected; the course may be acute (3 months) or chronic (4 years). One or many glands may be involved. The microscopical picture is not influenced by any of these factors.

Of the 22 fatal cases, (1) the gland architecture was replaced by a homogeneous mass of lymphoid cells in 18 cases (80%). Sinuses and germinal centers were distinguishable in 5 cases. (2) The capsule was invaded in 16 cases (72%). (3) The predominating lymphoid cell averaged 7-8μ in diameter and contained a somewhat clear nucleus with coarse chromatin particles irregularly distributed. (4) Irregularity in size and shape of these cells, denoting amœboid activity, was noted in 12 cases (54%). In these, the subsequent course was rapid; exitus occurring within a few months. (5) Mitoses were frequent in 18 cases (80%). (6) Endothelial hyperplasia, oval cells

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usually lining lymph spaces, was noticeable in 10 cases (45%). Eosinophilia was conspicuous in 6 cases (27%).

Of the four living cases, (1) the gland architecture was obliterated in two cases. (2) The capsule was infiltrated in two cases. (3) The cells appeared usually similar to those described above in the fatal cases. (4) No amœboid activity was noted. (5) Mitoses were numerous in two cases. (6) Slight endothelial hyperplasia was seen in two cases. (7) No eosinophiles were noted.

From the above data it seems that the four living cases, all of whom are reported "well" by their physicians, show glands which microscopically correspond to many of the malignant fatal cases. It appears, then, unwise to base a diagnosis upon the microscopical examination of a single gland or at least to offer a definite prognosis.

Lymphatic Leukæmia

We come, now, to lymphatic leukæmia, where a permanent increase in the number of lymphocytes in the circulating blood, accompanied by hyperplasia of the lymphoid elements, renders a diagnosis relatively simple. There occur, however, border line cases which make a brief survey of this group worth while.

Fifteen cases have been studied from the pathological records of The Johns Hopkins Hospital. A short summary of each follows:

Case 63.—G., white, male, age 57. Family and past history unimportant. Onset of present illness three months before admission with loss of weight, malaise, constipation, and chronic cough. Physical examination January 17, 1920, showed pallor, loss of weight, and dyspnœa. Cervical and axillary glands were palpable. Liver and spleen were enlarged. R. B. C. 1,400,000; Hb 24%; W. B. C. 840. Ninety per cent of the white cells were "smudges." Of those remaining, P. M. N. = 40%; S. M. = 30%; T. = 30%. Platelets decreased. Urine examination negative. Tubercle bacilli were found in the sputum. The patient received many transfusions to raise his blood count. By April 1 lung signs became prominent, anæmia progressed, and his general condition became worse. On April 22 four teeth were extracted. A few days previous to this his white count had been 17,000, but at once he developed a septic temperature, great numbers of staphylococci were cultured from his blood, and his white count went up rapidly until the day before his death, when it reached 42,000. Clinical impression: primary aplastic anæmia.

Autopsy 6244. *Anatomical Diagnosis.*—Chronic pulmonary tuberculosis with cavity formation and pleurisy with effusion; multiple pulmonary abscesses; œdema; splenomegaly and enlarged liver with lymphatic infil-

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trations; lymphatic infiltrations in kidney, bone marrow, and retroperitoneal lymph glands; staphylococcus septicæmia; infected splenic infarct and subphrenic abscess; small abscesses in liver and kidney; acute vegetative endocarditis, *et cetera.*

Body: Is that of a fairly large white man showing evidence of loss of weight. Cervical and axillary glands are enlarged. Liver and spleen extend below the costal margin. Right pleural cavity is obliterated by dense fibrous adhesions. *Heart:* Normal. *Lungs:* Tuberculous with cavities and effusion. *Spleen:* Weighs 1780 grams and shows an infected infarct. *Mesenteric lymph glands:* Markedly enlarged, dark red. On section yellow, opaque areas suggest caseation. *Gastro-intestinal tract:* Normal. *Pancreas:* Weighs 200 grams. *Liver:* Weighs 3250 grams and shows hemorrhages and small abscesses. *Adrenals:* Normal. *Kidneys:* Show abscesses. *Lymph glands:* Retroperitoneal glands appear similar to mesenteric glands; others only slightly enlarged. *Bone marrow:* Red.

Microscopical Pathology.—Lungs show tubercles. *Spleen:* Infiltrated with lymphocytes. *Mesenteric glands:* Are divided by fibrous trabeculæ separating homogeneous masses of normal or slightly enlarged lymphocytes. Hyperplastic germinal centers and dilated sinuses. *Liver:* Periportal infiltrations of lymphoid cells. Numerous necrotic foci and small abscesses. *Kidneys:* Lymphocytic infiltration and small abscesses. *Bone marrow:* Infiltrated with lymphoid cells. No normoblasts; numerous phagocytes.

Briefly, a middle aged man with various foci of infection develops suddenly, after his blood-forming apparatus has become exhausted, a tremendous lymphocytosis one week before death. At autopsy infiltration of parenchymatous organs and bone marrow with involvement of deep lymph glands is noted. Associated with these findings are evidences of a generalized infection. The large size of the liver and spleen would indicate that the lymphoid infiltrations had been present for some time. Whether the patient presented while in the hospital an aleukæmic state of lymphoid leukæmia stirred up shortly before death, or whether his sudden lymphocytosis was merely a response to a terminal infection, is difficult to decide.

Case 64.—Clarke H., white, male, age 69. For the past 40 years the patient has noticed slight shortness of breath following an attack of lead poisoning. Morphinism at 29, stopping at 49. Neisser infection at 19. The present illness began four months ago with a tumor mass in the lower right quadrant, constipation, loss of weight and strength. General swelling of lymph nodes began three months ago. One month ago a lump was felt in the upper abdomen. Physical examination, December 14, 1917, revealed general glandular enlargement, enlarged liver and spleen, emaciation, jaundice and ascites. A lymph gland removed from the neck was

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diagnosed as lymphosarcoma. Blood examination showed a slight secondary anæmia, W. B. C. 18,200, P. M. N. 63%, L. 10%, T. 2%, smudges 25%. X-ray showed a mass in the mediastinum. Wassermann negative. Another blood count December 17 reported that the lymphocytes appeared pathological with basophilic and vacuolated cytoplasm and large irregular nuclei. December 18 the patient died. Duration of illness five months.

Autopsy 5389. *Anatomical Diagnosis.*—Aleukæmic lymphatic leukæmia with general involvement of lymphoid tissue, spleen, kidneys and appendix.

Body: Is that of an emaciated white man 69 years old. Legs and ankles are œdematous. All superficial lymph glands are markedly enlarged. On opening the thorax the anterior mediastinum is occupied by a mass of enlarged glands which are firm and discrete and appear white and translucent on section. The axillæ are full of similar appearing glands. On opening the peritoneal cavity a considerable amount of straw-colored fluid is seen. The liver extends well below the umbilicus. The spleen is also greatly enlarged and is visible below the left border of the liver. Beneath the intestines is a large mass of glands. Similar nodules about the size of almonds are scattered through the mesentery. *Heart* and *lungs:* Negative. *Spleen:* Weighs 1680 grams. It is firm, gray in color and on section shows numerous white translucent areas scattered about amongst the Malpighian bodies. *Liver:* Weighs 5040 grams, is extremely large and firm. The cut surface shows diffuse irregular translucent patches between inconspicuous strands of pale brown tissue. *Kidneys:* Weigh 160 grams each. The capsules strip easily, leaving a smooth red-brown surface in which one or two yellowish opaque nodules are noted. *Intestines:* Show hyperplasia of Peyer's patches. The mesenteric glands are everywhere enlarged and are of the same appearance as the other lymph glands.

Microscopical Pathology.—Gland: Sections show a homogeneous mass of cells devoid of architecture. The capsule is not invaded, sinuses are indefinite, and the germinal centers are not seen. Due to amœboid activity, cells are extremely irregular in size, 6-12μ, and shape. Sometimes the nucleus is spindle formed, sometimes round, sometimes polymorphous. It is always vesicular and contains a few coarse chromatin granules. Mitotic figures are numerous. Normal lymphocytes are scattered about inconspicuously. *Spleen:* Shows about the Malpighian bodies and disseminated throughout the pulp cells lymphoid infiltration similar to that described above. *Liver:* Collections of these same cells are massed about the portal areas and are wandering between the hepatic cells of the lobules. Mitoses are frequent. *Kidneys:* A large sharply outlined nodule of infiltrating cells is seen in the cortex. *Intestines:* Lymphoid follicles are enlarged by collections of lymphoid cells quite similar to those seen in the other organs.

Briefly, a white male, 69 years old, comes to the hospital with enlarged inguinal glands which had been growing for four months. Physical examination December 14, 1917, revealed a general glandu-

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lar enlargement, enlarged liver and spleen. Blood count reports W. B. C. 18,200, with P. M. N. 63%, L. 10%, smudges 25%. The lymphocytes appeared pathological. Autopsy revealed a general glandular enlargement, infiltration of parenchymatous organs, but no invasive tumor. The predominating lymphoid cell appears extremely amœboid. This case might be classed as an aleukæmic state of lymphatic leukæmia.

Case 65.—White, male, age 46. Three years before admission the patient noticed a vesicular eruption over the face which soon disappeared. One year ago weakness, jaundice, and loss of weight became marked. Physical examination March 22, 1919, showed W. B. C. 4,800 with 90% lymphocytes. The patient grew worse and died April 6, 1919.

Autopsy 5867. *Anatomical Diagnosis.*—Lymphatic leukæmia with involvement of superficial and deep glands, spleen, liver and bone marrow; leukæmic ulcerative colitis.

This case with its atypical blood picture might well be classed with aleukæmic leukæmia.

Case 66.—White, female, age 19. Autopsy 754. *Anatomical diagnosis:* Acute leukæmia; swelling of spleen and deep lymphatic glands; red bone marrow; broncho-pneumonia; cloudy swelling of liver; infarcts of spleen and kidneys; swelling of intestinal follicles.

The cells, lymphoid in type, are quite regular, averaging 8μ in diameter.

Case 67.—W. M., age 65. Two weeks before death extreme pallor was noted. In the hospital no symptoms or signs were made out except a marked anæmia with an increase in the mononuclear cells.

Autopsy 1885. *Anatomical Diagnosis.*—Lymphatic leukæmia; bronchopneumonia; œdema of the lungs.

***Liver, spleen* and *kidneys* showed no lymphocytic infiltration. *Lymph glands:* Are only slightly enlarged. *Bone marrow:* The normal hemopoietic tissue is completely replaced by a homogeneous mass of lymphoid cells.**

This case, reported elsewhere by Reed, is an example, according to her, of acute leukæmia arising in the bone marrow and following so rapid a course that the parenchymatous organs and lymph glands had not yet become infiltrated.

Case 68.—White, female, age 23. Autopsy 148. *Anatomical diagnosis:* Lymphatic leukæmia with general glandular enlargement, involvement of parenchymatous organs and gastro-intestinal tract and bone marrow. Congenital syphilis of liver; etc.

The cells are regular, lymphoid type and average 8μ in diameter.

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CASE 69.—Black, female, age 40. Autopsy 608. *Anatomical diagnosis:* Lymphatic leukæmia; old operative wound; multilocular cysts of ovary (chloroform death); hydronephrosis and chronic diffuse nephritis; gallstones.

The intestinal follicles, liver and spleen, are extensively infiltrated. The cells are lymphoid in type, regular, and average 6μ in diameter.

CASE 70.—White, male, age 20. Autopsy 1397. *Anatomical diagnosis:* Blood picture of lymphatic leukæmia; general glandular enlargement; splenic tumor; anæmic infarction of spleen; anæmia of all viscera and fatty parenchymatous degeneration; lymphoid bone marrow; enlarged persistent thymus; ascaris lumbricoides.

General glandular enlargement is marked with an extensive infiltration of parenchymatous organs, bone marrow, heart and testes. Cells are lymphoid in character, regular, averaging 6μ in diameter.

CASE 71.—White, male, age 64. Autopsy 1471. *Anatomical diagnosis:* Lymphatic leukæmia with enlargement of all lymph nodes; infiltration of parenchymatous organs and bone marrow and gastro-intestinal tract. Streptococcus septicæmia.

Cells average 6μ in diameter and are regular.

CASE 72.—Black, female, age 21. Autopsy 2868. *Anatomical diagnosis:* General anæmia; general glandular enlargement; pigmentation of spleen and liver with hemorrhagic areas and focal necroses; lymphoid nodules in kidneys; hemorrhages in pericardium; hyperplasia of bone marrow; recent pregnancy; puerperal uterus with remnant of placenta; emphysematous and gangrenous vaginitis; diphtheritic and hemorrhagic cystitis; corpus luteum of pregnancy; cranial exostoses of pregnancy; hypertrophied breasts.

This case, with a general glandular enlargement and infiltration of parenchymatous organs and bone marrow, shows everywhere lymphoid cells regular in size (6μ) and shape.

CASE 73.—White, male, age 49. Autopsy 3680. *Anatomical diagnosis:* Lymphatic leukæmia with extensive involvement of spleen, mediastinal and retroperitoneal glands, liver and kidneys; bilateral hemorrhagic effusion into pleural cavities; lobar pneumonia; acute fibrinous pleurisy; etc.

This case, showing general glandular enlargement, involvement of parenchymatous organs, shows cells regular in size (6μ) and shape.

CASE 74.—White, male, age 2½. Autopsy 4094. *Anatomical diagnosis:* Lymphatic leukæmia; fatty degeneration of viscera; hemorrhagic necroses of liver; acute myocarditis; dilatation of heart; acute splenic tumor.

This case, with general glandular enlargement, involvement of parenchymatous organs and bone marrow, shows cells regular in size (6μ) and shape.

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CASE 75.—White, male, age 60. Autopsy 4677. *Anatomical diagnosis:* Lymphatic leukæmia involving lymph glands and parenchymatous organs; acute necrotizing and ulcerative colitis (His bacillus); gastric ulcer; etc.

This case, with general glandular enlargement, infiltration of parenchymatous organs, prostate and bone marrow, shows cells regular in size (6μ) and shape.

CASE 76.—White, male, age 51. Autopsy 4723. *Anatomical diagnosis:* Lymphatic leukæmia with hyperplasia of spleen, lymph glands and bone marrow; anæmia; multiple hemorrhages into lungs, spleen and kidneys; etc.

This case, with general glandular enlargement, infiltration of parenchymatous organs and bone marrow, shows cells regular in size (6μ) and shape.

CASE 77.—Patrick O'C., white, male, age 55. Family and past history unimportant. Present illness onset seven months before admission with dyspnœa, swelling of legs, loss of weight, and nodules in the inguinal region which have increased in size. Physical examination March 25, 1896, showed a large, full abdomen, generalized œdema, and enlargement of superficial lymph glands with palpable spleen and a mass in the region of the lumbar glands. Different blood counts are summarized at the end of the history. May 12, discharged after having developed a confluent papular eruption. One year later patient was admitted again with increased dyspnœa, œdema, and general weakness. The lymph glands were larger and the lumbar tumors were more noticeable. December, 1898, patient was admitted for the third time for exacerbation of the same symptoms. February 1, after a delirium which lasted several days during a terminal pneumonia, the patient died. His temperature was irregular with a final rise.

Blood Elements.	3-'96	5-'96	3-'98	12-'98	12-4-98	12-28-98	1-26-'99
R. B. C. (in millions)	3.8	3.1	3.3	2.7	....	2.2	2.1
Hb. %	37	50	60	40	....	35	30
W. B. C. (in thousands)	24	67	25	44	72	112	139
P. M. N. %	....	4.5	13	3.2	2	2	18
P. M. E. %	....	....	....	2	....	5	1
Lymphocytes %	....	95	84	88	....	94	80
T. %	....	.6	3	6	....	....	....

Autopsy 1261. *Anatomical Diagnosis.*—Lymphatic leukæmia with general hyperplasia of lymph glands and inguinal and retroperitoneal tumor formations; infiltration of hepatic vessels, portal and hepatic veins; nodules in spleen; involvement of pancreas and lungs; lymphoid bone marrow.

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Body: **Is that of an emaciated white man, 166 cm. long. In each inguinal region a large tumor mass of nodular character is seen, over which the skin is tense and cyanotic. The tumors extend upward toward Poupart's ligament and are continuous with masses in the pelvic and abdominal cavities. On opening the peritoneal cavity the intestinal loops are displaced by large tumor masses within the peritoneal cavity. Tumors on the right and left side of the pelvis come together and push the bladder before them, producing a funnel-shaped opening in which the lower part of the sigmoid and upper part of the rectum are lying. The mesentery of the small intestine is shortened, due to a large tumor mass which is pushing forward from behind.** ***Spleen:*** **Is enlarged. The Malpighian bodies are distinct.** ***Liver:*** **Is not enlarged and shows no tumor nodules. Whitish accumulations are noted in the periportal area following the portal vein throughout its ramifications.** ***Kidneys:*** **Are the seat of a marked hydronephrosis. The ureters are included in the tumor growth from the lumbar region to the pelvis.** ***Inguinal tumors:*** **Measure on either side about 40 x 30 x 30 cm. They are developed from the inguinal glands, pass directly into the large tumors of the pelvis and retroperitoneal region which are themselves composed of large lymph glands. In this vicinity there is an invasion of the cellular tissue covering the ilia. The union to these parts makes the separation of the tumor difficult. This mass extends upward to include the peripancreatic glands and preaortic chain.** ***Bronchial glands:*** **Are much enlarged and pass continually into the large glands of the neck.** ***Axillary glands:*** **Enlarged.** ***Stomach*** **and** ***intestines:*** **Apparently normal.** ***Bone marrow:*** **Hyperplastic.**

Microscopic Pathology.—**The inguinal and retroperitoneal** ***tumors*** **are composed of solid masses of lymphoid cells regular in size (7μ) and shape.** ***Parenchymatous organs:*** **All show extensive infiltration of a similar type of cell.** ***Bone marrow:*** **The marrow cells are completely replaced by a homogeneous mass of lymphoid cells.**

Briefly, a white man aged 55 years, came to the hospital March 25, 1896, with a seven years' history of dyspnœa, œdema, and loss of weight, with rapidly growing tumor masses in the inguinal regions. General glandular enlargement soon became marked. During three years of observation the W. B. C. increased from 24,000 to 112,000. Small lymphocytes were relatively constant at 80 or 90 per cent. It was during the last month, however, that the W. B. C. rose from 33,000 to 112,000 and were accompanied by an enormous increase in size of the inguinal tumors. At autopsy these masses were seen to invade skin, periglandular tissue, fascia and periosteum covering the ilia, retroperitoneal tissues and pancreas. A general glandular enlargement and an infiltration of the parenchymatous organs and bone marrow were also noted. Everywhere the tumor cells were of the lymphoid type, regular

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and similar in size, shape and general morphology. So one might regard this case first as doubtful, later as certain chronic lymphatic leukæmia, terminating with local invasive tumor masses.

CHART NO. 5.—SUMMARY OF LYMPHATIC LEUKÆMIA

Case.	Size of cell.	G.G.E.	Paren. org.	Bone marr.	Other org.	Blood.	Tumor.
63	6μ	Deep	+	+	0	+ (terminal)	0
64	6μ	+	+	?	0	±	0
65	6μ	+	+	+	Intestine	±	0
66	8μ	Deep	+	+	0	+	0
67	8μ	Deep	+	+	0	+	0
68	8μ	+	+	+	Intestine	+	0
69	6μ	+	+	?	Intestine	+	0
70	6μ	+	+	+	Heart	+	0
71	6μ	+	+	+	0	+	0
72	6μ	+	+	+	0	+	0
73	6μ	+	+	?	0	+	0
74	6μ	+	+	+	0	+	0
75	6μ	+	+	+	Prostate	+	0
76	6μ	+	+	+	0	+	0
77	6μ	+	+	+	0	+	+

Cases 63, 64, 65, showed at autopsy hyperplastic changes in the lymphoid tissue. Clinically, however, the blood could not definitely be termed leukæmic although the morphology and relative number of lymphocytes were altered. An excellent discussion of similar cases by Fraenkel and Sternberg may be found in the Proceedings of the German Pathological Society for 1912. The society recognized the intimate relationship between such "pseudo-leukæmic" cases and true lymphatic leukæmia, mentioned examples where the one had progressed into the other, referred to cases where at autopsy the two conditions were indistinguishable, and concluded that the term "pseudo-leukæmia" was superfluous and should be abandoned. Cases 66 and 67, with leukæmic blood pictures, showed at autopsy infiltration of the parenchymatous organs and bone marrow. But lymphoid hyperplasia was confined to mesenteric and retroperitoneal glands. Cases 68 to 77, with leukæmic blood, general hyperplasia of lymphoid tissue, and infiltration of parenchymatous organs and bone marrow, are quite typical. Case 77, observed for over three years, gradually developed large invasive tumor masses of the inguinal and retroperitoneal glands.

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Hodgkin's Disease

For a thorough and complete account of this condition refer to Ziegler, Die Hodgkinsche Krankheit. It will be sufficient for me to describe and group 11 cases taken from the autopsy records of The Johns Hopkins Hospital.

Case 78.—White, male, age 55. Autopsy 492. *Anatomical diagnosis:* Hodgkin's disease involving axillary, supraclavicular, retroperitoneal and inguinal glands, spleen and liver; rupia on left arm; streptococcus septicæmia.

Microscopic Pathology.—Gland: Sinuses and germinal centers obliterated; lymphocytes greatly reduced; striking increase in connective tissue stroma. Endothelioid cells and giant cells numerous. Few eosinophiles. *Liver:* Sections show islands of typical Hodgkin's tissue. *Spleen:* Shows infiltration with Hodgkin's tissue.

Case 79.—White, male, age 27. Autopsy 566. *Anatomical diagnosis:* Hodgkin's disease; general glandular enlargement; nodules in spleen and liver; jaundice, ascites, hydrothorax.

Microscopic Pathology.—Gland: Sinuses and germinal centers obliterated; lymphocytes markedly reduced; connective tissue increased; endothelioid and giant cells very numerous; no eosinophiles. *Liver:* Areas of typical Hodgkin's tissue are seen.

Case 80.—White, female, age 32. Autopsy 741. *Anatomical diagnosis:* Hodgkin's disease; with general glandular enlargement and involvement of liver and spleen; cirrhosis of liver; etc.

Microscopic Pathology.—Gland: Sinuses and germinal centers obliterated. Great reduction of lymphocytes and increase in connective tissue. Endothelioid cells and giant cells numerous. No eosinophiles. *Liver:* Shows similar collections of cells near the portal areas.

Case 81.—Black, female, age 25. Autopsy 3032. *Anatomical diagnosis:* Hodgkin's disease; general glandular enlargement; nodules in lungs, spleen and liver; pressure on trachea, aorta, œsophagus and lungs; dilatation and hypertrophy of right ventricle; chronic passive congestion of lungs, liver and kidneys; anasarca; ascites; hydrothorax; hydropericardium; ulceration of larynx and stomach.

Microscopic Pathology.—Gland: Germinal centers and sinuses obliterated; great reduction of lymphocytes and increase in connective tissue; endothelioid cells and giant cells very numerous; no eosinophiles. *Spleen* and *liver:* Show similar infiltrations.

Case 82.—White, male, age 12. Autopsy 1658. *Anatomical diagnosis:* Hodgkin's disease involving all glands; infiltration of spleen, liver and pericardium. Tuberculosis of lymph glands, spleen and liver; miliary tuberculosis of kidneys and lungs; tuberculous ulcers in larynx and intestines.

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Microscopic Pathology.—Gland: Germinal centers and sinuses obliterated; lymphocytes reduced; connective tissue stroma greatly increased; endothelioid cells and giant cells very numerous; no eosinophiles. Tubercles are seen. *Other organs:* Show infiltrations similar to those described above and tuberculous lesions.

Case 83.—White, male, age 18. Autopsy 3146. *Anatomical diagnosis:* Hodgkin's disease; involvement of all lymph glands, spleen and liver; chronic passive congestion of viscera; tuberculosis of lungs and liver.

Microscopic Pathology.—Gland: Germinal centers and sinuses are distinguishable; lymphocytes are somewhat reduced. Connective tissue stroma is increased; endothelioid cells and giant cells are numerous; many eosinophiles. *Liver:* Shows tubercles.

Case 84.—White, female, age 55. Autopsy 1375. *Anatomical diagnosis:* Hodgkin's disease; general glandular enlargement with invasion of cervical tissues; nodules in anterior and posterior mediastinum compressing trachea, œsophagus, etc.; nodules in liver and spleen; cirrhosis of liver; chronic nephritis; etc.

Microscopic Pathology.—Glands: Sinuses and germinal centers are obliterated. Lymphocytes are greatly reduced and connective tissue stroma is abundant. Many endothelioid and giant cells; no eosinophiles. *Spleen* and *liver:* Show similar accumulations.

Case 85.—(This case is reported in detail by Longcope.) Autopsy 2220. *Anatomical diagnosis:* Hodgkin's disease; general glandular enlargement; invasion of anterior mediastinum, trachea, and both lungs; involvement of spleen.

Microscopic Pathology.—Gland: Germinal centers and sinuses obliterated; lymphocytes reduced; connective tissue stroma markedly increased; endothelioid cells and giant cells very numerous. Few eosinophiles.

Case 86.—Black, male, age 15. Autopsy 2351. *Anatomical diagnosis:* Hodgkin's disease; general involvement of lymph glands with invasion of chest; nodules in liver, spleen and lungs.

Microscopical Pathology.—Gland: Germinal centers and sinuses obliterated. Lymphocytes reduced; connective tissue greatly increased; endothelioid cells and giant cells are numerous. Few eosinophiles.

The nine cases described are typical examples of Hodgkin's disease. They all present a general glandular enlargement with involvement of liver and spleen. Tuberculosis was present in two cases; three cases showed invasive tumor masses associated with the mediastinal or cervical glands.

Microscopically, (1) obliteration of normal architecture, (2) appearance of lymphoid cells, (3) decrease in normal lymphocytes, (4)

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increase in stroma (5) and diffuse endothelioid hyperplasia, with large irregular mononuclear and giant cells, were constant. (6) Eosinophiles were present in three cases.

CHART NO. 6.—SUMMARY OF TYPICAL HODGKIN'S CASES

				Glands: Microscopic pathology.					
Case.	G. G. E.	Tumor.	Liver. Spleen.	Obliterated architecture.	Lymphoid cells.	Normal lympho.	Conn. tiss.	End. cells. Giant cells.	Eosinophiles.
78	+	0	+	+	+	Reduced	++	++	+
79	+	0	+	+	+	Reduced	++	+++	0
80	+	0	+	+	+	Reduced	++	++	0
81	+	0	+	+	+	Reduced	++	+++	0
82	+ TBC.	0	+	+	+	Reduced	++	++	0
83	+ TBC.	0	+	0	+	Reduced	++	++	+
84	+	Chest	+	+	+	Reduced	++	++	0
85	+	Chest	?	+	+	Reduced	++	++	0
86	+	Chest	+	+	+	Reduced	+++	++	+
Total	9		8	8	9	9	9	9	3

Three atypical cases subjected to radium, difficult to classify, will be described.

CASE 87.—Smith N., white, male, age 66. Family and past history negative except for attacks of hematemesis 18 years ago which persisted irregularly for nearly a year. At this time he lost weight and developed a scaly itching eruption which appeared on the arms. It recurred each September, usually disappearing in cold weather. However, he has had no recurrence of the hematemesis. Present illness began three weeks before admission with dysuria, swollen cervical lymph glands and irregular fever. Physical examination, November 30, 1914, showed a generalized scarlatinaform eruption with scaly epidermis. Cervical glands were very large. Also, there was a general glandular enlargement. Liver and spleen were palpable. Wassermann negative. Examination of blood: Hb 90%, W. B. C. 10,000 with lymphocytes 8% and eosinophiles 33%, P. M. N. = 52%. An excised lymph gland was diagnosed Hodgkin's disease. X-ray therapy was instituted, but the patient became much worse, and spleen and liver enlarged. Examination of blood shortly before death showed Hb 91%, W. B. C. 12,800, P. M. N. 73%, P. M. E. 1%, lymph. 13%, T. 11%.

Autopsy 4245. *Anatomical Diagnosis.*—Hodgkin's disease with general glandular enlargement, extensive involvement of solitary follicles of the intestine, liver and spleen; hypertrophy of the prostate; etc.

Body: Is that of an emaciated white man. *Heart* and *lungs:* Normal. *Spleen:* Weighs 900 grams. The parenchyma is reddish brown. *Liver:* Weighs 2600 grams, is mottled and shows numerous grayish nodules scattered throughout the parenchyma. *Intestines:* The solitary follicles of the

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large intestine are markedly enlarged. *Lymph glands:* There is a general glandular enlargement, but each gland is discrete, definitely encapsulated, soft, juicy and mottled, appearing red with opaque background.

Microscopic Pathology.—Gland: Appears as a homogeneous tumor mass. The predominating cell is spread evenly throughout, invading capsular lymphatics, sinuses, occupying diffusely cortex and medulla of the gland. No germinal centers are seen. These cells are irregular in size (6-12μ) and shape. Nuclei are quite vesicular with coarse chromatin granules. Mitoses are very frequent. Larger endothelioid cells, often phagocytic, are scattered diffusely amongst the lymphoid cells. Many of these cells possess two or three nuclei. Normal lymphocytes are greatly reduced in number; many of them show pycnotic and fragmented nuclei. *Spleen:* Cells similar to those described above surround arterioles and are scattered uniformly throughout the pulp. The giant cells and phagocytic forms are numerous. *Liver* and *kidney:* Show similar infiltrations.

Briefly, the patient, a white man 66 years old, came to the hospital with enlarged cervical glands which had begun to swell three weeks before admission. Physical examination, November 30, 1914, showed a general glandular enlargement and enlarged liver. Blood examination showed an eosinophilia of 33 per cent. An excised gland was diagnosed Hodgkin's disease. After two weeks' treatment with X-ray, the eosinophiles dropped to 1 per cent, liver and spleen increased in size, and the patient's condition continued worse until his death five weeks after onset. Autopsy revealed a general glandular enlargement, infiltration of spleen and liver, but no invasive tumor. Microscopically, an irregular lymphoid cell is conspicuous. Many are undergoing degeneration; many are being phagocytized. Endothelioid cells of all sizes, irregular in outline, are numerous; many giant cells and phagocytic cells are seen.

Case 88.—Charles G., white, male, age 28. Family and past history are unimportant. Present illness began June 13, 1913, with a small lump on the left side of neck. Six months later glands began to enlarge on both sides of the neck and in axillæ. Physical examination May 1, 1914, showed a general glandular enlargement associated with loss of weight. Liver and spleen were not palpable. Blood examination practically normal. Wassermann negative. Gland removed from neck was diagnosed Hodgkin's disease. After one month of radium treatment all glands increased markedly in size and the patient died June 7, with respiratory symptoms.

Autopsy 4141. *Anatomical Diagnosis.*—Hodgkin's disease with involvement of spleen and all lymph glands. Œdema of left upper extremity. Pleural and peritoneal effusions; atelectasis; congestion and œdema of lungs; fibrous pleural adhesions.

Body: Is that of an emaciated white man. Superficial veins over chest and shoulders are markedly swollen. Tumor mass involves right and left

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sides of neck, invades the posterior pharynx and base of tongue. The mesenteric and retroperitoneal glands are enlarged. A mass of tumor tissue surrounds the pancreas and each kidney. The mediastinum is packed with huge glands continuous with those in the abdomen. Axillary and inguinal glands are enlarged. The peritoneal and pleural cavities contain a quantity of thick creamy fluid which does not have the odor or appearance of pus. *Heart:* Normal. *Lungs:* In the upper left lung is seen an invasion of the tumor mass. *Spleen:* Weighs 280 grams and shows on section numerous small white nodules scattered diffusely throughout the organ. *Stomach:* Shows great enlargement of lymph nodules beneath the mucosa and enlargement of the gastric lymph glands. *Pancreas:* Is ensheathed by tumor tissue. *Liver:* Weighs 1850 grams and shows on section normal architecture. *Kidneys:* Weigh 160 grams each, appear pale and show a few small nodules. *Pelvic organs:* Negative. *Neck organs:* Show great enlargement of all the glands. The thyroid is infiltrated by tumor masses. *Intestines:* Show hypertrophy of the lymphoid follicles.

Microscopic Pathology.—Gland (removed before radium treatment): Appears as a homogeneous cellular mass with no sinuses, no germinal centers, no separation into cortex and medulla. Lymphocytes, although normal in appearance, are reduced in number. Instead, one sees many larger mononuclear cells, amœboid, with vesicular nuclei. Endothelioid cells, 12-14μ in diameter, with large, irregular vesicular nuclei, are scattered thickly throughout the section. Many contain two or three large nuclei. Eosinophiles are numerous. Reticular cells and connective tissue trabeculæ are not especially prominent. *Tumor:* Is composed of a solid mass of cells supported by delicate reticulum, few blood vessels and fibrous trabeculæ. The cells are very striking. They measure from 6-12μ in diameter and are probably amœboid because of their irregularity in outline. Cytoplasm is quite prominent. Nuclei are vesicular, contain coarse chromatin granules and often show mitotic figures. Frequently, these cells have two or three nuclei. Many of them are phagocytic, containing in their swollen cytoplasm fragments of lymphocytes. *Spleen:* Shows similar infiltrating cells. *Liver* and *kidney:* Sections show no infiltrations.

Briefly, a white male, aged 28 years, came to the hospital with a history of general glandular enlargement beginning one year before admission. Physical examination, May 1, 1914, showed, besides enlargement of all superficial glands, an increase in P. M. N. count to 79 per cent, with reduction of lymphocytes to 2 per cent. After three weeks of radium treatment the glands had increased in size, respiratory difficulty had become pronounced and the patient died. Autopsy revealed a tumor of the cervical glands invading the pharynx, general glandular enlargement, and infiltration of the spleen. Again, as in

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the previous case the predominating cell is apparently of lymphoid type but irregular endothelioid cells and giant cells are very numerous.

Case 89.—Sarah M., white, female, age 45. Family and past history are negative. Her general health had been excellent until sixteen days before her death, when she developed, suddenly, chills and fever which persisted throughout the course of her acute illness. The onset was associated with a general glandular enlargement and a cutaneous skin eruption. Physical examination showed a marked leukocytosis with 50% eosinophiles. During the last week of her life an anæmia became marked, pneumonia developed associated with an increase in polymorphs to 76%.

Autopsy 6036. *Anatomical Diagnosis.*—Hodgkin's disease; general glandular enlargement; splenomegaly; nodules in lungs, liver and kidneys; eczema; acute catarrhal bronchitis; hydrothorax; pleural adhesions.

***Microscopic Pathology.—Gland:* Sinuses and germinal centers are practically obliterated. The stroma extends as diffuse, inconspicuous, spindle cells throughout the gland substance. The cells are somewhat reduced in number; different types are noted. Normal lymphocytes are not frequent, but many larger lymphoid cells are present. Large irregular endothelioid cells, some phagocytic, others containing two or three nuclei, are conspicuous. *Spleen, liver* and *kidneys:* Show similar infiltrations.**

Briefly, a white woman, aged 45 years, came into the hospital with a two weeks' history of chills and fever, general glandular enlargement, and a morbilliform cutaneous eruption. Examination showed, besides, a severe bronchitis and a marked leukocytosis with 50 per cent eosinophiles. As the pulmonary condition progressed, the eosinophiles dropped and the P. M. N. rose to 76 per cent. At autopsy a general glandular enlargement with infiltration of the parenchymatous organs was noted. Lymphoid cells predominate; irregular endothelioid cells with large nuclei are scattered about conspicuously. Some are phagocytic; some are multinucleated.

CHART NO. 7.—SUMMARY OF ATYPICAL HODGKIN'S CASES

Case.	G.G.E.	Tumor.	Liver. Spleen.	Oblit'ed arch'ure.	Lymphoid cells.	Normal lympho.	Conn. tiss.	End. cells. Giant cells.	Eosinophiles.
87	+	0	+	+	+++	+	±	+	+
88	+	Neck	+	+	++	+	±	+	++
89	+	0	+	+	++	+	±	+	+

In these acute cases the lymphoid cells predominate. The total number of cells is not decreased, the stroma is not conspicuous. A few endothelioid cells, giant cells and phagocytes are noted.

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CLINICAL CASES

From the clinical standpoint the same questions of interest in lymphosarcoma apply to Hodgkin's disease. Thirty-three cases will be described.

CASE 90.—Y., white, male, age 37. S. P. 25650. General glandular enlargement one year. Operation, removal of gland for diagnosis. *Microscopic study:* Morphology obliterated; areas of necrosis; stroma increased; total number of cells reduced. Normal lymphocytes reduced; many lymphoid cells. Diffuse scattering of large endothelioid cells; few giant cells. Many eosinophiles.

CASE 91.—C. S. P. 25537. Enlarged cervical glands. Operation, removal of gland for diagnosis. *Microscopic study:* Morphology obliterated; stroma not increased; cells not reduced; clumps of normal lymphocytes near capsule; many lymphoid cells. Few large endothelioid cells with prominent nuclei; few giant cells. Few eosinophiles.

CASE 92.—C. S. P. 25528. *Microscopic study:* Morphology obliterated; stroma not increased; cells not reduced. Many normal lymphocytes; many lymphoid cells. Few large endothelioid cells; few giant cells. Very many eosinophiles.

CASE 93.—M. S. P. 25119. *Dead. Microscopic study of gland:* Morphology obliterated; stroma somewhat increased; cells not reduced in number. Normal lymphocytes evident; many larger lymphoid cells; many lymphocytes undergoing disintegration; few large endothelioid cells; few giant cells. Few eosinophiles. Many phagocytic wandering cells.

CASE 94.—S. S. P. 24643. *Dead. Microscopic study of gland:* Morphology obliterated; stroma somewhat increased; cells somewhat reduced. Lymphocytes in clumps; many lymphoid cells; many lymphocytes undergoing disintegration. Many endothelioid cells; few giant cells. Many eosinophiles. Many phagocytic wandering cells.

CASE 95.—S., white, female, age 20. S. P. 24560. *Dead. Microscopic study of gland:* Morphology obliterated; great increase of stroma; fibrosis; cells somewhat reduced. Few lymphoid cells. Many large endothelioid cells; very many large giant cells (6-8 nuclei); remarkable eosinophilic infiltration.

CASE 96.—R., white, female, age 27. S. P. 24457. *Microscopic study of gland:* Morphology obliterated; great increase in stroma; fibrosis; areas of necrosis; reduction of cells. A few lymphocytes are scattered about; few lymphoid cells. Many large endothelioid cells; many giant cells; many eosinophiles.

CASE 97.—H., white, female. S. P. 24348. In 1914 an enlarged lymph gland of the neck was removed and diagnosed tuberculosis. In 1919 a cervical gland from a large mass in the neck was removed. The patient

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died shortly afterward. *Microscopic study of gland:* Morphology obliterated; increase in stroma; fibrosis; areas of necrosis; no reduction of cells. Lymphocytes conspicuous; few lymphoid cells. Few large endothelioid cells; many giant cells. Few eosinophiles.

CASE 98.—B., white, male, age 37. S. P. 24223. *Dead. Microscopic study of gland:* Morphology obliterated; increase in stroma; some fibrosis; no necrosis; cells reduced. Few lymphoid cells. Many endothelioid cells and giant cells. Very many eosinophiles.

CASE 99.—G. S. P. 24199. *Dead. Microscopic study of gland:* Morphology obliterated; slight increase in stroma; cells not reduced in number. Many lymphoid cells. Many large endothelioid cells; many giant cells. No eosinophiles.

CASE 100.—H., white, male, age 34. S. P. 24099. Abdominal tumors and general glandular enlargement one year. *Microscopic study of gland:* Morphology obliterated; slight increase in stroma; cells reduced in number; few lymphoid cells. Many endothelioid cells. Few giant cells. Many eosinophiles.

CASE 101.—F. S. P. 23514. *Dead. Microscopic study of gland:* Morphology obliterated; increase in stroma; cells reduced in number. Few lymphoid cells; many endothelioid, many giant cells. Many eosinophiles. Many polymorphs.

CASE 102.—S. S. P. 23474. *Dead. Microscopic study of gland:* Morphology obliterated; almost complete fibrosis; hyalinization; few cells remaining in clumps. No lymphocytes; few lymphoid cells. Few endothelioid cells; few giant cells; few eosinophiles.

CASE 103.—D. S. P. 22301. *Dead. Microscopic study of gland:* Morphology obliterated; no necrosis; increase in stroma; cells reduced in number. Lymphocytes reduced; numerous lymphoid cells. Few endothelioid cells. Few giant cells. Few eosinophiles.

CASE 104.—D., white, male, age 21. S. P. 20934. *Dead.* Cervical tumors six years; recurred after operation. Duration seven years. *Microscopic study of gland:* Architecture obliterated except for a few crowded germinal centers and clumps of lymphocytes pushed toward the periphery. Stroma increased. Predominating cell of lymphoid type; few normal lymphocytes. Many large endothelioid cells; many giant cells. Many eosinophiles.

CASE 105.—C. S. P. 20923. *Microscopic study of gland:* Morphology obliterated; increase in stroma; lymphoid and large endothelioid cells are present in equal numbers; many giant cells in clumps. Many eosinophiles.

CASE 106.—R. S. P. 19279. General glandular enlargement. *Dead* one + years after onset. *Microscopic study of gland:* Morphology obliterated; increase in connective tissue; no decrease in number of cells. Pre-

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dominating cell of lymphoid type. Many normal lymphocytes scattered about. Large endothelioid cells are frequent. Few giant cells. No eosinophiles.

CASE 107.—W. S. P. 18046. Symptoms of general glandular enlargement. *Dead* two years after onset. *Microscopic study of gland:* Morphology obliterated; gland reduced to fibrosed, hyaline mass with few islands of cells. No necrosis. Predominating cell of lymphoid type. Great endothelial hyperplasia in the form of small vessels; few large endothelioid cells; few giant cells. No eosinophiles.

CASE 108.—T., white, male, age 28. S. P. 16728. Symptoms of general glandular enlargement. *Dead* six months after onset. *Microscopic study of gland:* Morphology obliterated; increase in connective tissue; cells reduced in number. Lymphoid and endothelioid cells present in equal numbers. Many giant cells; no eosinophiles.

CASE 109.—N. S. P. 16626. *Microscopic study of gland:* Morphology obliterated; increase in connective tissue stroma; no decrease in cells; predominating cell of lymphoid type; few normal lymphocytes; few large endothelioid cells and giant cells. No eosinophiles. Many fragmented nuclei; some phagocytes.

CASE 110.—C., white, male. S. P. 16427. Enlarged cervical glands. *Dead* four years after onset. *Microscopic study of gland:* Morphology obliterated; increase in stroma; decrease in number of cells. Lymphoid cells, endothelioid cells and reticulum cells are present in equal numbers. Numerous giant cells and eosinophiles.

CASE 111.—R., white, male, age 28. S. P. 15730. *Dead* two years. *Microscopic study of gland:* Morphology obliterated; diffuse increase in stroma; number of cells somewhat reduced; few lymphoid cells. Stroma cells and endothelioid cells are present in equal numbers. Few giant cells. Many eosinophiles.

CASE 112.—T., black, female, age 35. S. P. 15205. Enlarged cervical glands two and a half years. *Microscopic study of gland:* Morphology obliterated by connective tissue which leaves clumps of cells in small islands surrounded by connective tissue bands. Fibroblasts and endothelioid cells predominate; few lymphoid cells; few lymphocytes; few giant cells.

CASE 113.—R., white, female, age 41. S. P. 14599. Enlarged cervical glands. *Dead* ten months after onset. *Microscopic study of gland:* Morphology obliterated; large part of gland is fibrosed, leaving cells in small islands. Predominating cell of lymphoid type; few normal lymphocytes. Few large endothelioid cells; few giant cells. Many eosinophiles.

CASE 114.—P., black, male, age 13. S. P. 14399. *Microscopic study of gland:* Morphology obliterated; some increase in stroma; no reduction of cells. Predominating cell of lymphoid type; few normal lymphocytes. Few large endothelioid cells, giant cells and eosinophiles.

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CASE 115.—B., white, female, age 19. S. P. 12743. Enlarged cervical glands. *Microscopic study of gland:* Morphology obliterated. Connective tissue bands reduce cells to small islands. Predominating cell of lymphoid type. Few endothelioid cells; few giant cells. No eosinophiles.

CASE 116.—L., white, male, age 28. S. P. 12389. Symptoms of general glandular enlargement with large liver and spleen. *Microscopic study of gland:* Morphology obliterated; increase in connective tissue stroma. Predominating cells are lymphoid and endothelioid types. Lymphocytes are infiltrating the periglandular tissue. Few giant cells; no eosinophiles.

CASE 117.—F., white, female, age 44. S. P. 11199. *Dead* one year after onset. *Microscopic study of gland:* Morphology obliterated; connective tissue increased. Large numbers of polymorphs throughout the gland. Few lymphoid cells and lymphocytes. Moderate number of endothelioid cells; few giant cells and eosinophiles.

CASE 118.—B., white, female, age 32. S. P. 10964. *Dead* two + years. *Microscopic study of gland:* Morphology obliterated; stroma increased; cells reduced. Predominating cell of lymphoid type; few normal lymphocytes. Many oval endothelial cells scattered about. Few irregular endothelioid cells; few giant cells; few eosinophiles.

CASE 119.—White, male. S. P. 9622. *Dead* two years. *Microscopic study of gland:* Morphology obliterated; stroma increased by fibrous bands and by profuse reticular cell proliferation. Reticulum cells, lymphoid, and endothelioid cells are present in about equal numbers. Few giant cells; many eosinophiles.

CASE 120.—White, male, age 63. S. P. 8322. Symptoms of general glandular enlargement for two and a half years. *Microscopic study of gland:* Morphology obliterated; diffuse increase in stroma; cells reduced in number. Lymphoid, reticulum, and endothelioid cells are present in equal numbers.

CASE 121.—S., white, female, age 15. S. P. 9162. 1908 tonsillectomy with excision of cervical glands. Diagnosed at that time tuberculosis and Hodgkin's disease. *Well* seven years. *Microscopic study of gland:* Morphology altered. Few germinal centers seen. Caseated areas and typical tubercles are noted; one or two tuberculous giant cells. Remainder of gland shows reduction of cells, increased stroma. The predominating cell is of lymphoid type. Endothelioid cells are numerous. Few giant cells and eosinophiles.

CASE 122.—P., white, male, age 22. S. P. 17907. 1912, diphtheria and enlarged cervical glands. 1915, glands reappeared after tonsillectomy. At this time a cervical gland was removed for diagnosis. *Well* eight years. *Microscopic study:* Morphology obliterated; increase in coarse connective tissue trabeculæ; cells not reduced in number. Lymphoid cells predominate; few normal lymphocytes. Many large endothelioid cells. Few giant cells. No eosinophiles.

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CASE 123.—G., white, male, age 55. S. P. 19156. 1914, malaria and enlarged cervical glands. Removal of gland for diagnosis, 1916. Radium treatment since then. *Well* four and a half years. *Microscopic study of gland:* Morphology obliterated; great increase in stroma and connective tissue. Normal lymphocytes predominate. Few scattered endothelioid cells; no giant cells. No eosinophiles.

CHART NO. 8.—SUMMARY OF CLINICAL CASES OF HODGKIN'S DISEASE

		Gland: Microscopic study.									
Case.	Patient.	Morphology.	Necrosis.	Stroma.	Number cells.	Lymphocytes.	Lymphoid.	End'oid cells.	Giant cells.	Eosinophil.	Predom. cells.
90	W.M. 37	0	+	+	—	—	++	++	+	+	Oid: End
91	.....	0	0	±	±	±	+	+	+	+	Oid
92	.....	0	0	±	±	—	+	+	+	+++	Oid
93	.....	0	0	+	±	—	+	+	+	+	Oid
94	.....	0	0	+	±	—	+	+	+	++	Oid: End
95	W.F. 20	0	0	++	—	—	±	++	++	+++	End
96	W.F. 27	0	+	++	—	—	+	++	++	++	End
97	W.F.	0	+	+	±	±	+	+	++	+	Oid: End
98	W.M. 37	0	0	+	—	—	±	+++	++	+++	End
99	.....	0	0	+	±	—	++	+++	++	0	Oid: End
100	W.M. 34	0	0	+	—	— —	++	++	+	++	End
101	.....	0	0	++	—	— —	+	+++	++	+	End
102	.....	0	0	+++	— —	— —	++	+	+	+	Oid
103	.....	0	0	++	—	—	++	+	+	+	Oid
104	W.M. 21	0	0	+	—	—	+++	+	+	+	Oid
105	.....	0	+	+	—	—	++	++	+	+	Oid: End
106	.....	0	0	±	±	—	+++	+	+	0	Oid
107	.....	0	0	+++	— —	—	++	+	+	0	Oid
108	W.M. 28	0	0	++	—	—	++	++	+	0	Oid: End
109	.....	0	0	++	±	—	++	+	+	0	Oid
110	W.M.	0	0	++	—	—	++	++	+	+	Oid: End
111	W.M. 28	0	0	+++	—	—	±	++	+	++	End
112	B.F. 35	0	0	+++	— —	—	±	++	+	0	End
113	W.F. 41	0	0	+++	— —	—	+++	+	+	++	Oid
114	B.M. 13	0	0	+	±	±	++	+	+	+	Oid
115	W.F. 15	0	0	+++	— —	—	++	+	+	0	Oid
116	W.M. 28	0	0	+	—	—	++	++	+	0	Oid: End
117	W.F. 44	0	0	+	—	—	+	+	+	+	Oid
118	W.F. 32	0	0	++	— —	±	++	++	+	+	Oid
119	W.M.	0	0	++	—	— —	++	++	+	++	Oid: End
120	W.M. 63	0	0	++	—	—	++	++	+	0	Oid: End
Total	31 cases	31	4	29	22	27	27	31	31	22	Oid: End
121	W.F. 15	±	0	++	—	±	++	+	+	0	Oid
122	W.M. 22	0	0	++	±	±	+++	++	+	0	Oid
123	W.M. 55	0	0	++	+	±	+++	+	0	0	Oid
Total	3 cases	2	0	3	2	0	3	2	2	0	Oid

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Nineteen cases are dead; 12 cases, although no report has been received, were so far advanced that they may be classed with the fatalities, bringing the total to 31. Three cases are living, one after 8 years, one after 7 years, and one after 4½ years.

All ages are affected; the course may be acute (6 months) or chronic (4½ years). One or many glands may be affected.

Of the 31 fatal cases, (1) the normal architecture was obliterated in 31 cases (100%). (2) The stroma was definitely increased in 29 cases (93%). In six of these, dense bands of connective tissue had so far replaced the pulp that the cellular elements appeared as small isolated nodules. (3) The cells were reduced in number in 22 cases (70%). (4) The number of normal lymphocytes was diminished in 27 cases (86%). (5) Lymphoid cells larger than the normal lymphocyte were present in 27 cases (86%). (6) Endothelioid cells with large irregular nuclei containing a nucleolus and punctate chromatin granules were conspicuous in 31 cases (100%). (7) Endothelioid giant cells were present in every case (100%). (8) Eosinophiles were present in 22 cases (70%). (9) Lymphoid cells predominated in 13 cases (40%); endothelioid cells in 7 cases (23%); and in 11 cases (36%) lymphoid and endothelioid cells seemed to be present in about equal numbers.

Of the three living cases, (1) Normal architecture was obliterated in two cases. (2) Increase in stroma, reduction of the total number of cells and of normal lymphocytes were constant. (3) Larger lymphoid cells, always predominating, were very abundant in all cases. (4) Endothelial cells, sometimes oval, lining lymph channels, sometimes large and irregular, were evident. (5) Giant cells, infrequent, were present in two cases. (6) No eosinophiles were noted.

The 31 fatal cases present, therefore, a microscopical picture which may be readily diagnosed. Lymphoid cells with little stroma are abundant in the early cases. Stroma increases, cells become less numerous, endothelioid cells become more conspicuous as the process advances. The three living cases do not seem to fall into this group, but resemble the four cases of so-called lymphosarcoma which are still well. In all of these cases the lymphoid cell was the most conspicuous. The total number of cells, however, was decreased. Irregular endothelioid cells and giant cells were infrequent; eosinophiles were not noted.

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Discussion

From the foregoing description of 123 cases it seems possible to draw a number of interesting observations.

First of all I wish to emphasize the close relationship between leukosarcoma, lymphosarcoma, and lymphatic leukæmia. Three leukosarcoma cases studied in the Johns Hopkins Department of Pathology presented a blood picture of lymphatic leukæmia, general involvement of the lymphatic system, infiltration of the parenchymatous organs and bone marrow associated with an invasive mediastinal tumor. One case beginning as a localized tumor of the chest developed a typical lymphatic leukæmia after X-ray treatment. Glands enlarged all over the body, liver and spleen descended below the costal margin. The subsequent findings at autopsy were similar to those in the cases mentioned above. It seems then, that leukosarcoma combines the features of lymphosarcoma and lymphatic leukæmia and that a localized lymphosarcoma may under certain conditions become generalized and, with a blood picture of lymphatic leukæmia, may terminate as a leukosarcoma. Very important in this connection is the mode of spread of the lymphosarcoma group. From charts No. 2 and 3 it seems that lymphosarcoma, regardless of its primary site, extends in a characteristic manner first by local infiltration and later by the blood stream to parenchymatous organs, lymph glands, bone marrow, etc. At this stage only the negative blood findings differentiate the case from leukosarcoma and only the blood and the presence of a local infiltrating mass differentiate it from lymphatic leukæmia. Finally, in the lymphatic leukæmia chart No. 5, one may see a similar mode of progression. The first cases showing no increase in the number of blood lymphocytes presented at autopsy hyperplastic lymphoid tissues with generalized infiltrations. Other cases with a positive blood picture showed more or less localized lymphoid envolvement. The main group is quite typical but the last case on the chart developed, during the course of the leukæmia, large infiltrating masses in the inguinal regions. It appears then, that in the leukæmia group some cases closely resemble certain types of lymphosarcoma, others approach leukosarcoma.

Microscopically, the lymphocytic infiltrations of the organs in these diseases differ in quantity but not in quality. Distant lymph nodes appear the same in leukosarcoma as in lymphosarcoma and leukæmia;

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the parenchymatous organs and even the bone marrows are indistinguishable. Although the cell varies in size and shape in the several cases, it still retains its lymphoid character.

It appears not unlikely, then, that leukosarcoma, lymphosarcoma, and lymphatic leukæmia are different manifestations of the same disease. In early life the primary focus may be in the small intestine or mediastinum. It then runs a rapid fatal course spreading locally or generally (lymphosarcoma), occasionally to terminate with manifestations of lymphatic leukæmia (leukosarcoma). Later in life the focus may be anywhere and the course is more protracted. Extension, however, occurs in a similar manner. In many ways the disease is quite comparable with tuberculosis which, in the young, localizes in the chest or intestine, later to become spread more diffusely and, in adult life, assumes many odd forms attacking kidney, uterus, skin, etc.

Next I wish to say a word about the nature of this disease. From the preceding paragraph it may be seen that its local manifestations and mode of spread are not at all comparable to a malignant tumor with its metastases but simulate more closely the progress of an infectious disease. The site of origin is determined by an infiltrating mass of lymphoid cells not in themselves destructive but merely pushing aside normal tissue elements. Its mode of spread as a diffuse periportal infiltration, accumulation about the Malpighian bodies, scattered cells separating normal kidney tubules and glomeruli, homogeneous collections of cells in the bone marrow and other tissues, certainly does not find its parallel in the biology of any known tumor.

From observations by Lewis and Webster upon the activities of lymphocytes in tissue culture (normal, tuberculous, lymphosarcomatous, Hodgkin's and leukæmic lymph glands were cultured and the activity of the lymphocytes studied), the following points may be valuable. (1) The lymphocyte in normal and pathological lymph nodes observed in tissue culture is actively amœboid at body temperature, proceeding in a definite and characteristic manner for several days. (2) It responds to various chemical and bacterial substances. Observing many fixed sections from autopsies in which the lymphocytes, elongated and spindle shaped, were similar to those in culture, it seems altogether probable that amœboid activity may take place on the part of the lymphocyte *in vivo*.

This lymphoid infiltration then, variously designated as leukosarcoma, lymphosarcoma, and lymphatic leukæmia, may best be ex-

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plained as a response to some chemotactic agent derived from a living organism. So long as this substance remains confined, the accumulation of lymphocytes is local; but the presence of this substance in any part of the body, parenchymatous organs, glands, bone marrow, etc., produces in that area an infiltration of lymphocytes.

A minor point of some prognostic significance might be mentioned at this time. Several clinical cases where a lymph node had been removed for diagnosis showed microscopically evidence of amœboid activity on the part of the lymphocytes. All of these cases (12) died within a few months.

Hodgkin's disease, a reticulo-endothelial proliferative process, in contrast to leukosarcoma, lymphosarcoma and lymphatic leukæmia which are lymphocytic proliferative processes, may be diagnosed microscopically and is probably a distinct entity.

From the clinical standpoint, until a definite etiological agent has been discovered, these conditions will remain little more than diagnostic problems. Lymphosarcoma cannot always be diagnosed microscopically and in the early cases it is unwise to give a certain prognosis. Hodgkin's disease, on the other hand, may be diagnosed from the microscopical examination of a single gland and a definite prognosis may be offered.

Seven atypical cases living and well from 2 to 11 years after examination are quite similar microscopically. The more or less homogeneous mass of lymphoid cells suggests some benign form of chronic lymphadenitis. Associated with these cases is frequently a so-called transient "infectious mononucleosis" in the blood characterized by an increase in the number of lymphoid cells.

Conclusions

1. It seems probable that leukosarcoma, lymphosarcoma, and lymphatic leukæmia are different manifestations of the same disease.

2. The term "lymphadenosis, leukæmic or aleukæmic" would express this idea and simplify the classification until a definite etiological agent is found.

3. This disease is not a neoplasm but a direct response on the part of lymphocytes to a chemotactic influence exerted by the disease causing agent. The presence of this substance in any tissue or organ produces there a local accumulation of lymphoid cells.

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4. Diagnosis and prognosis of this disease in its early stage are difficult from the microscopical examination of a single gland because of its resemblance to certain types of benign lymphadenitis.

5. Evidence of amœboid activity on the part of the lymphocytes is indicative of a rapid fatal course.

6. Hodgkin's disease, a distinct entity, may be diagnosed and accurately prognosed from the microscopical examination of a single gland.

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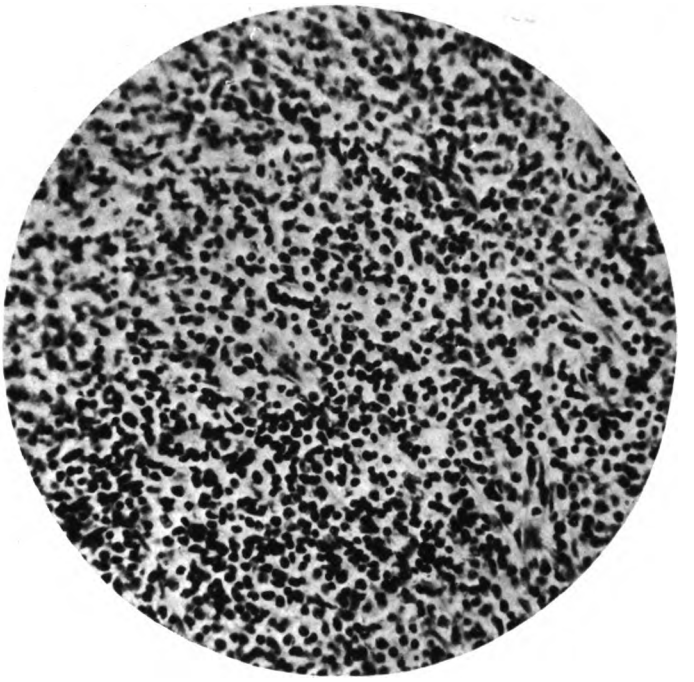

FIG. 1.—*Case 58:* Lymphosarcoma. Lymph gland. Patient dead; eight months' duration. Note amœboid lymphocytes with numerous mitoses, endothelial hyperplasia, and phagocytosis.

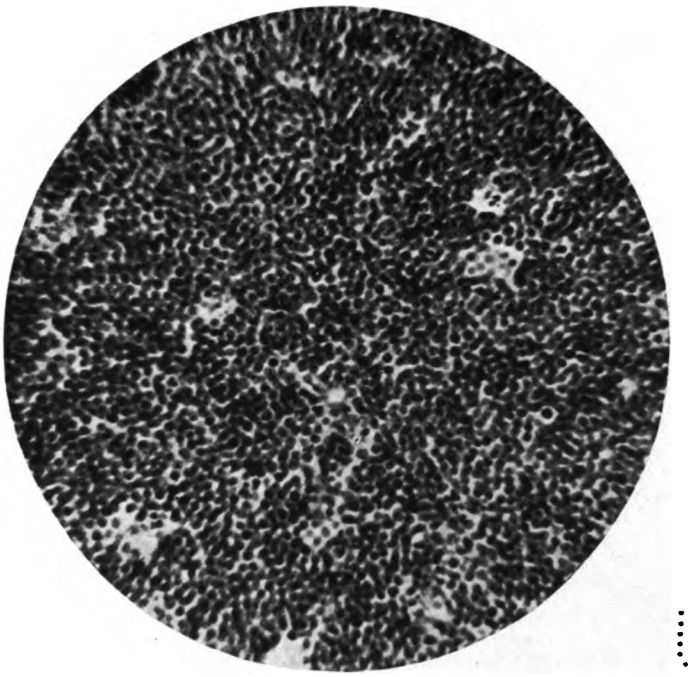

FIG 2.—*Case 3:* Leukosarcoma. Lymph gland removed before patient developed leukæmia. Notice the diffuse overgrowth of lymphocytes regular in size and shape.

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FIG. 3.—*Case 1:* Leukosarcoma. Lymph gland. The lymphocytes are regular in size and shape, supported by a delicate stroma.

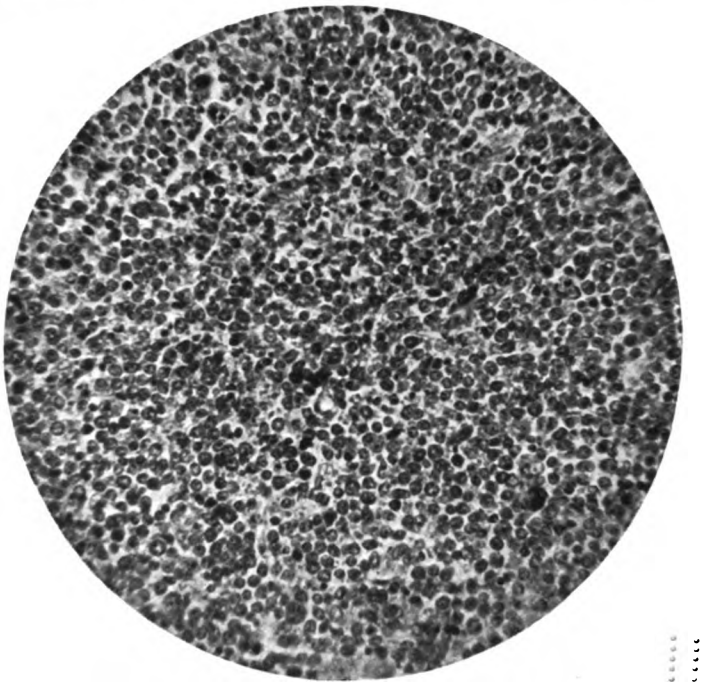

FIG. 4.—*Case 87:* Lymph gland. Atypical acute Hodgkin's disease with X-ray treatment and death five weeks after onset. The predominating lymphoid cell is large and amœboid with a somewhat vesicular nucleus. Mitoses are frequent. Large endothelioid cells are filled with nuclear particles.

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FIG. 5.—*Case 104:* Hodgkin's disease. Lymph gland. Typical example of a relatively early case: many lymphoid cells, with scattered endothelioid cells, and giant cells are noted.

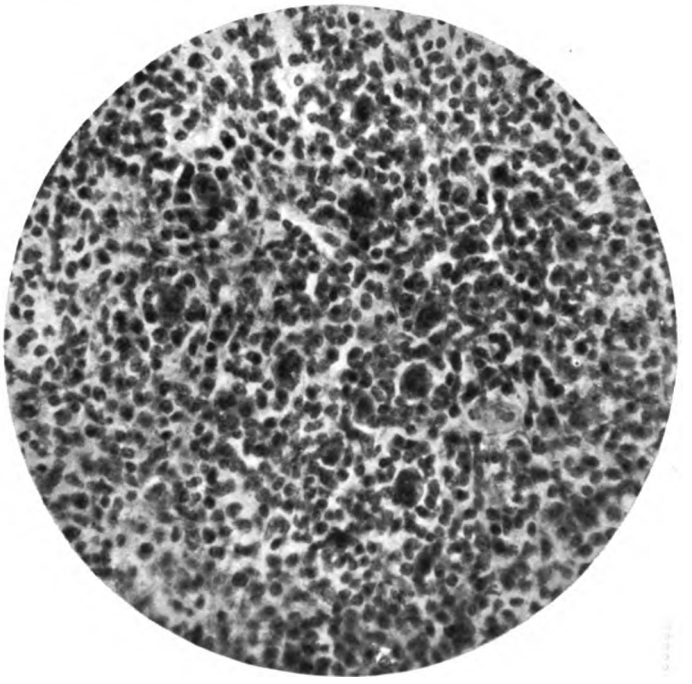

FIG. 6.—*Case 99:* Lymph gland. Typical Hodgkin's disease with lymphoid cells still abundant. Stroma is more conspicuous, endothelioid cells and giant cells are numerous.

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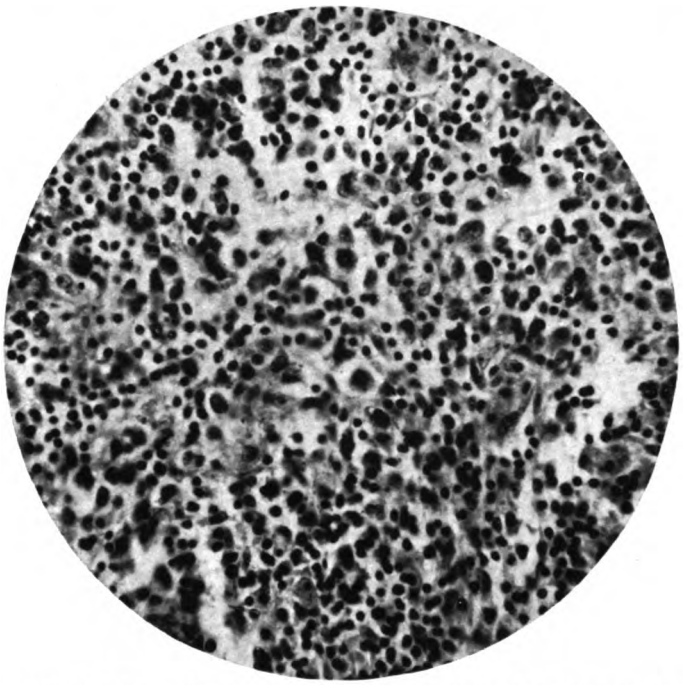

FIG. 7.—*Case 105:* Lymph gland. Hodgkin's disease well advanced. The lymphoid cells have decreased in number until they are scarcely more frequent than the prominent endothelioid cells and giant cells. Increase in stroma and endothelial hyperplasia are conspicuous.

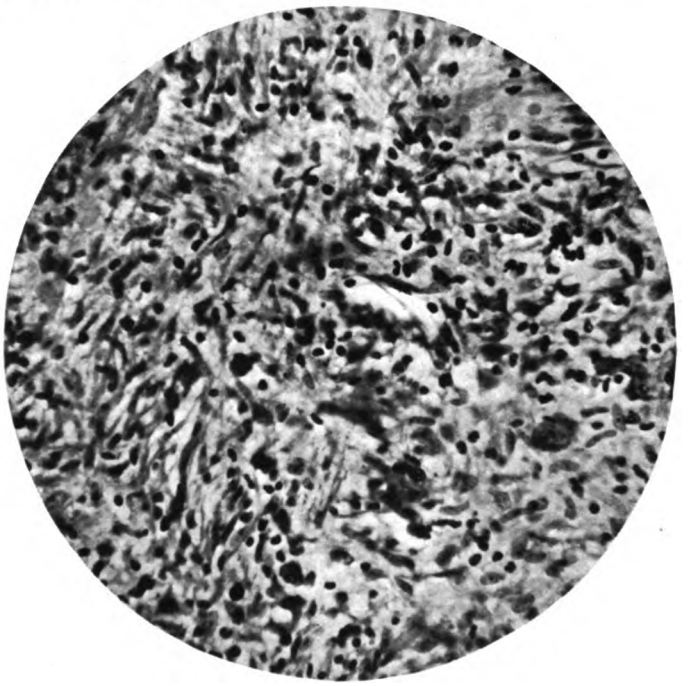

FIG. 8.—*Case 112:* Lymph gland. Advanced Hodgkin's disease. The small island of lymphoid cells, endothelioid cells, and giant cells is surrounded by dense stroma of connective tissue.

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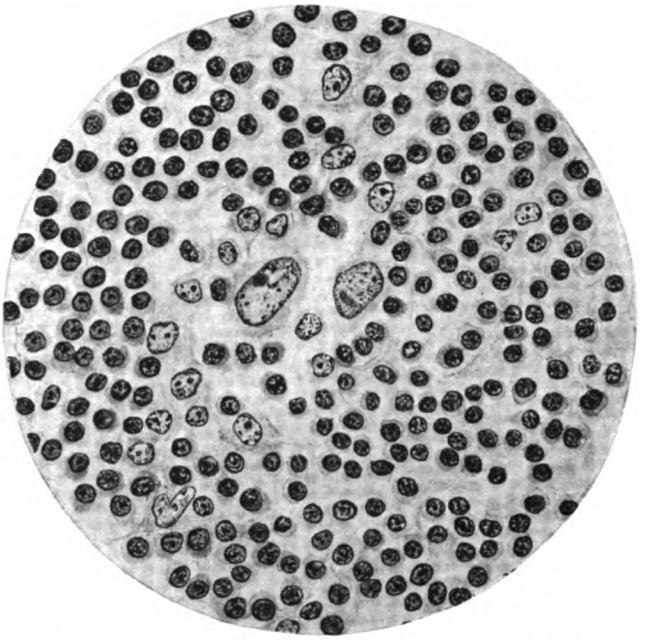

FIG. 9.—*Case 59:* Lymph gland diagnosed lymphosarcoma. Well eleven years. Note homogeneous mass of lymphoid cells regular in size and shape. Nuclei are deep staining with no mitoses. Note large endothelioid cells.

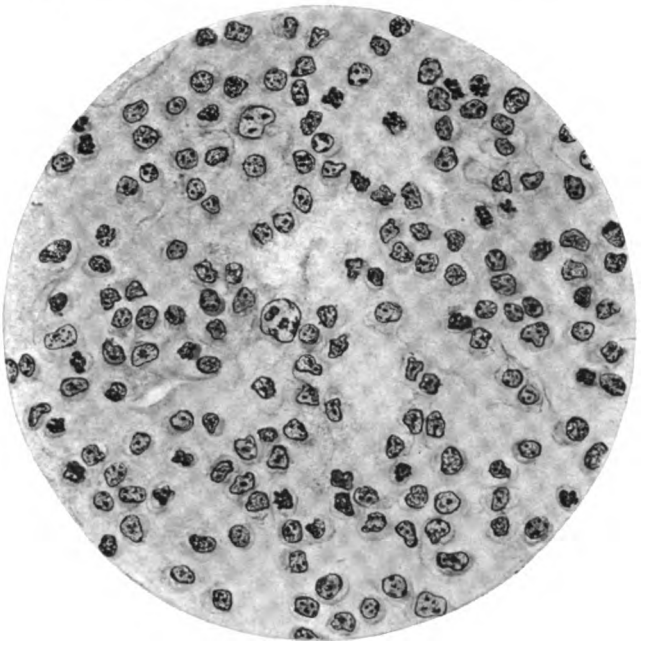

FIG. 10.—*Case 60:* Lymph gland. Diagnosed lymphosarcoma. Well four years. Note lymphocytes slightly irregular in size and shape.. The nuclei are somewhat vesicular and frequently show mitotic figures. An occasional endothelioid cell is noted.

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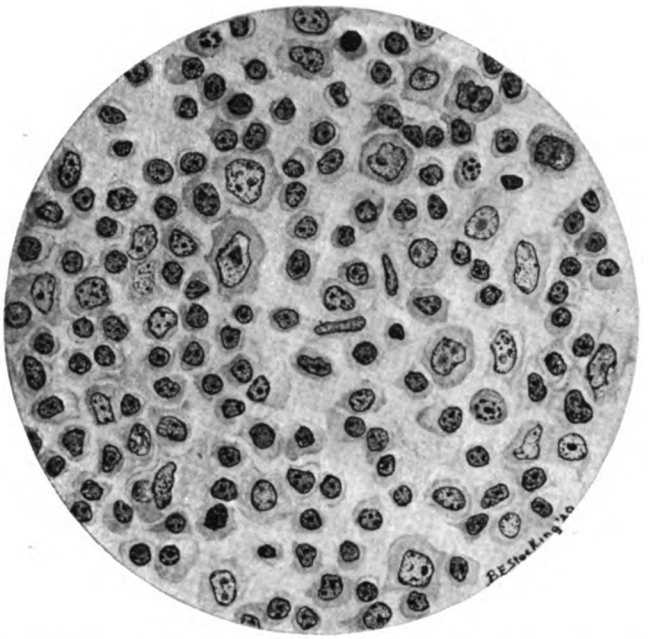

FIG. 11.—*Case 61:* Lymph gland. Diagnosed lymphosarcoma. Well three years. Many lymphocytes contain pycnotic nuclei. Endothelioid cells are numerous in this area.

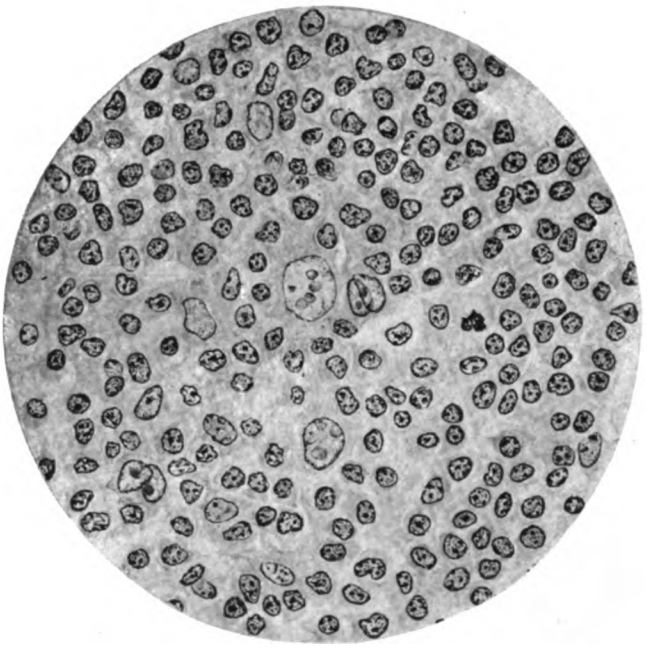

FIG. 12.—*Case 122:* Lymph gland. Diagnosed Hodgkin's disease. Well five years. Note lymphoid cells, quite regular with slightly vesicular nucleus. A few endothelioid cells are seen.

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INVESTIGATION OF THE CENTRAL NERVOUS SYSTEM

BALTIMORE
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1920

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PART I

Investigation of the Central Nervous System Methods and Instruments

BY
R. H. CLARKE, M.A., M.B.

PART II

Atlas of Photographs of the Frontal Sections of the Cranium and Brain of the Rhesus Monkey (*Macacus Rhesus*)

BY
R. H. CLARKE, M.A., M.B., AND E. E. HENDERSON, B.A., M.B., F.R.C.S.
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INTRODUCTION

It is due to those who are interested in this work to express my regret for the delay that has occurred in publishing a promised description of a new stereotaxic instrument. Something in the way of excuse may be recognized in the following pages, when it is realized that the details explained, besides many which are omitted, had to be worked out, not only on paper, but in mechanical constructions which were submitted to experiment and modified in accordance with the results, involving much time, labor and expense.

One difficulty in constructing a complicated instrument is to secure the services of a maker who combines the requisite skill and appliances with leisure to carry out the work. The time of such men is valuable and they are not attracted by the uncertainty and difficulty of experimental construction. Such obstacles have been responsible for much delay; nevertheless, I had completed and tested an instrument and an illustrated description of it was ready for the press several years ago, but, at the last moment, the publication was postponed for the following reasons. The rectilinear instrument which is described and illustrated in these pages is constructed, as its name implies, on a rectilinear principle, and the movements of the needle, directed by guides, are controlled and measured by scales engraved on these guides or attached to them. To extend the range of these movements, to help the operator to avoid important structures in the brain and to reach any selected point by the most convenient route, or by more than one, the rectilinear movement was supplemented by an arrangement which provides for an inclination of the needle at various angles. But to direct it with accuracy, to know the exact position of the point at any inclination and at the same time, to make the required corrections for variations in the size of different heads, in three dimensions, was a matter of some difficulty. Calculations in the course of an operation are objectionable and I adopted a mechanical method of attaining these objects with a two-dimensioned indicator, which is figured in Plates XXV-XXVI and explained in Chapters III and IV. It soon became evident that an extension of this method to a

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three-dimensioned indicator and a needle with universal movement would offer great advantages, but I did not see my way to a satisfactory design until after the machine referred to was finished, and though a good many parts of it are still retained, many modifications and additions were necessary, involving the construction of what is practically another instrument.

Now that both patterns are completed and can be compared, the advantage of the improved form will be recognized, though it may not supersede the previous one for all purposes. However, as these instruments are costly, I could not recommend anybody to purchase one with the probability of its being quickly superseded and I was obliged to defer the publication of the description till the last, and I hope, the final form was completed. It may be objected that there is no finality in these things, that the last pattern will suggest another and so on indefinitely. This is of course true of details which must always be susceptible of improvement until perfection is attained, but machines reach what may be called a final stage when they effect their object as well as can be reasonably expected, and such a stage may be claimed for the present instrument, which satisfies all reasonable requirements, and can be recommended to experimental neurologists for the investigations it has been designed to promote.

The rectilinear machine described here is the second of the kind which I have designed; some of my readers may have seen a description of the earlier one, in a joint paper with Sir Victor Horsley,[1] introductory to an unpublished account of an investigation of the cerebellum, for which it was employed. Since then, a few investigators have used similar instruments copied from it, for various parts of the brain, and in spite of mechanical defects and the disadvantage of applying it without a complete series of charts, with fairly good results. At the same time, it is no criterion of the method to employ it under these conditions and I have advised enquirers to wait for the new instrument and the earlier parts, at any rate, of the atlas of sections of the cranium of the cat and monkey, which Mr. Henderson and I are now publishing.

It is of course an advantage to be able to refer to sections in three planes, but a single series will furnish the essential data for directing the needle and with either of the instruments described here and the earlier parts of the atlas, any one will be in a position to undertake an investigation of the brain in the cat or monkey if he wishes.

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The delay which has occurred, though unfortunate in some respects, has enabled me to introduce a few additions, which may enlarge the scope and utility of the method and will be described in this paper.

Those who have used the first instrument will find the later one a great improvement, but must not expect mathematical accuracy which is unattainable, as no animal's brain is constructed on such lines, but with a little practice and care he will find that he can reduce the inevitable error to small proportions.

Having reached something like finality in the evolution of the instrument I found it difficult to decide upon the alterations to be made in the description which had been completed to a certain point; much of it required to be re-written, but it was doubtful what to omit. If the cost of the earlier and the improved pattern were approximately the same, I should recommend the latter and be content with a short allusion to the first. I hoped to be able to append an approximate estimate of the comparative cost of the two machines, but this is difficult to obtain, because much depends on the number required, which it is impossible to predict, though the demand cannot be large, and I should imagine that the final instrument will cost two or three times as much as the rectilinear pattern.

As nearly all the essential parts of the first machine are used with the later improvements there is very little disadvantage incurred by getting the former to begin with and procuring the additional parts subsequently if required. There are many experiments for which the rectilinear machine serves very well and for such the plan suggested appears advisable. At any rate, it is desirable to give a full description of both instruments to enable the reader to draw his own conclusions, especially with reference to the work he proposes to undertake. To the descriptions and illustrations I propose to add directions for use and explanations which I hope will make the procedure sufficiently clear to enable the beginner to embark upon it without any special teaching.

Besides affording a substitute for mutilating operations, which are repulsive and not attended with results that justify them in the laboratory or hospital, a contingent advantage may be secured by facilitating the operative procedure essential to experimental investigation and enlisting the co-operation of medical men who are interested in scientific neurology, but have been deterred from supplementing clinical observations with experimental research by the want of special

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training which they considered essential. For performing the operations required with the instrument it is not so, and the need of fresh workers in this field is urgent. Considering our ignorance of elementary anatomical and physiological data, the course and connections of tracts, the functions of large centers, not to speak of smaller but important nuclei, the vast amount of indispensable work requiring no exceptional skill, the fascination of the subject, and the harvest to be gathered, the slow progress from the dearth of investigators is deplorable. Certainly, there are no direct pecuniary inducements, but probably an increasing number of medical men would be willing to devote some of their leisure to these objects if they realized their importance and inducements.

In criticizing what appear to me defects in present methods of intracranial surgery, my observations do not in any way apply to the operators, who are called upon to act in circumstances which admit of no delay. They cannot wait for the improvements they may desire, but must make the best of such means as are available, whether they are satisfactory or not, and for imperfections in methods and means we must all accept a share of responsibility, as it has always been open to any of us to suggest improvements.

I had made arrangements for the publication of this work and the charts of the cranium of the rhesus in the *Journal für Psychologie und Neurologie*[1] in which the two first parts of the atlas (of the cat) have already appeared. But the outbreak of the European war arrested the progress of this arrangement, besides leading to the closure of the laboratory in which I have always worked and depriving me of the services of the instrument maker on whom I depended for the completion of certain small additions and alterations to the machine which are required.

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PART I

Investigation of the Central Nervous System

Methods and Instruments

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INVESTIGATION OF THE CENTRAL NERVOUS SYSTEM

METHODS AND INSTRUMENTS

By R. H. CLARKE, M. A., M. B.

CHAPTER I

A PRELIMINARY REVIEW OF THE SCOPE AND APPLICATION OF THE METHOD

The purpose of the method and instruments described in the following pages is to give such practical effect as may be possible to the principle of substituting mechanical for visual direction of needles and similar fine instruments for intracranial operations, whether they are required for anatomy, physiology, or surgery, in the hope of ultimately reducing to small proportions the mutilation which exposure of the structures of the brain entails.

Topography, Uniformity.—The topographical basis of the method depends on the measurement of structures from central section planes in three dimensions, determined by prominent anatomical features of the cranium. It is evident that, unless the position and relations of the planes, determined in this way, are reasonably constant, the method cannot be trustworthy. This objection is frequently raised and neurologists are not easily convinced of such uniformity of structure in the brains of different animals of the same species, nor in different men. Of the latter, I am not yet in a position to speak from experiment, as my work on this subject has been confined to the lower animals, especially the cat and rhesus monkey, but, within the limits of my experience, uniformity increases as we ascend the scale of cranial development and it would be a contradiction of the apparent rule if the relations of cerebral structures proved to be less constant in man than in the monkey or cat. . The matter can be definitely decided only by the comparison of a large number of measurements and it would occupy too much space to produce even those which are available here; but the issue is fundamental and it is necessary

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to offer sufficient preliminary evidence to encourage those who are interested in the question to put it to the proof of practical experiment, when they will find in their results the most satisfactory corroboration of the claim advanced. It may be mentioned, in the first place, that one of the greatest obstacles to the recognition of the evidence of uniformity is due to the prominent position and great interest attached to the convolutions of the brain. Every neurologist is impressed by their importance, familiar with the details of their arrangement and structure and appreciates their topographical value, but, at the same time, realizes that their regularity and symmetry are not constant enough for the requirements of accurate measurement and it seems at first very improbable that any part of the brain can be free from the defects he has so often observed in these structures. When, however, we consider the development of the pallium and that the convolutions are folds produced by the confinement of its extending area by unyielding walls, it may appear more remarkable that the irregularities are no greater and that the arrangement is generally as symmetrical as we find it. We could hardly expect that folds so produced would be constant enough to serve as bases of accurate measurement, nor should we anticipate that defects in their symmetry would furnish a criterion for estimating the degree of uniformity exhibited by the central structures of the brain. Rather, if *a priori* considerations have any weight, we should expect a marked difference and that, in an area which is the seat of extensive growth and expansion and subject to very considerable variations of size, the relations of parts would be affected to a far greater degree than in structures closely connected with the base of the skull, where growth is slow and comparatively slight, and variations are restricted to small proportions. Such a conclusion is strongly supported by the positive evidence of observation and measurement. It is most obvious in coronal sections where the symmetry of corresponding structures of the brain-stem to the median sagittal plane is remarkable and also of practical value, as this plane is one of the bases of measurement. Of all zero planes, it is the most easily defined and owing to the bilateral structure of the brain the most natural and obvious landmark. Anatomically, its position is marked, superficially and in deep structures, by numerous features which can be easily recognized and it can also be determined by bisecting transverse diameters through corresponding points on both sides of the cranium. Both methods can

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be employed to corroborate one another, which, as a rule, they do. If there is any discrepancy, it is generally due to some difference, chiefly peripheral, in the development of the hemispheres and in case of doubt, for central structures at any rate, anatomical features, such as the raphé and the median division between corresponding points, are the surest guides. Such discrepancies, however, are neither frequent nor considerable, and the sagittal zero plane, determined in either way, is a satisfactory landmark for the brain stem and adjacent structures. Still more important and not less trustworthy, as a base of measurement, is the **interaural line**, passing from the center of one meatus to the other. The meatus is accurately centered by ear cones, which fit the conical ends of the ear pivots, and these are perforated in their long axis to serve as guides for the drill, which is used in the preparation of chart sections, to define the line. As the same ear cones and pivots are used to support the head in the frame for operations, and measurements are reckoned from the centers of the cones, the same line is defined for charts and operations by the same means. Thus, the interaural line defines the central intersection of the basi-horizontal and frontal zero planes; the distal definition of the former is determined by the lowest point of the lower margin of the orbit, and the frontal zero plane, perpendicular to the horizontal, extends from the same line to the vertex. The interaural line is, therefore, the focus and central zero of measurement, and as the principal structures of the brain which now require investigation are in its neighborhood, its accuracy is essential and far more important than the distal definitions of the zero planes, and, fortunately, in the cat and monkey it is a constant and trustworthy guide. I have drilled this line, through cones fitted in the meatuses, on both sides, in a very large number of cats' heads, and have been surprised at its regularity; as a rule, the drill grooves the free surface of the pons in the median sagittal line. The drills used were 14-wire gauge, 1.8 mm. in diameter, and on an average the depth of the groove is about half the diameter of the drill; but it is rare for the latter to perforate the pons without breaking its surface, or to pass without touching it. As the diameter of the drill is less than 2 mm., a variation of 1 mm. is sufficient to produce either of these results; hence, an error of 1 mm. is rare and a much greater one is not likely to occur in regions near the interaural line and measured from it, or from the frontal or horizontal zero planes which it defines. In the rhesus,

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the interaural line traverses the pons about its middle; there is no definite feature at this point comparable to the free surface in the cat and slight variations cannot be recognized so readily, but, judging by measurements to neighboring structures, I believe it to be as constant and trustworthy a guide.

Thus, if adjustment of the ear cones is carefully conducted, in the central regions of the brain of both these animals, an error of more than 1 mm. is unusual and it is commonly less; hence, the bases of measurement are sufficiently accurate for experimental operations and it appears unlikely that they will prove less accurate in man.

Our object might be compared with that of a marksman, assuming that we are aiming the needle at a target with a 2 mm. bull's-eye. A good performer with a modern rifle considers that, if all circumstances are favorable, with the stipulated number of shots he may hope to score a "possible," getting somewhere on the bull every time, but that if the wind is strong, or the light bad, or he is at all unsteady, he will not be so fortunate. Similarly, although under favorable conditions, in a series of experiments with the instrument, an operator may succeed in getting the needle within a 2 mm. circle every time; nevertheless, a slight error of measurement or some defect of symmetry in an animal will spoil his average. Much, however, depends upon the weapon, and as with the rifle, so with the instrument, there is a good deal of difference between the old and the new.

Defective Methods.—We have sacrificed opportunities of progress in the anatomy, physiology and surgery of the brain, by too ready acquiescence in the assumption that we must remain dependent on the visual sense for every species of intracranial operation. Like many accepted convictions, its foundations are open to criticism and it is remarkable that its claims to credit have not been seriously challenged long ago.

Inaccessibility of the Brain.—It is difficult to imagine a region more inaccessible to vision than the deep structures of the brain. An organ of almost inconceivable complexity, not absolutely solid nor yet fluid, but exhibiting some of both qualities, slung on membranous supports, in an impervious bony capsule, which is never restored when once it has been destroyed to give access to the structures it protects, and in every part, bone, membranes and brain richly supplied with blood contained in vessels, of which some are inaccessible or difficult to control for the arrest of hæmorrhage. These conditions make it

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impossible to expose the deep ganglia without serious mutilation, hæmorrhage and shock, which not only hinder the attainment of our object, but rob it of much of its value when it is secured. Instead of a clear view of the structures we find a stained and mangled mass, in which brain is scarcely distinguishable from blood-clot, landmarks are obliterated, structural relations confused and topographical precision impossible.

When we reflect on the extent of these difficulties we may well wonder, not that so little has been accomplished, but rather that so much has been achieved. We must recollect, however, that in the past there was a somewhat wide field for research in comparatively superficial structures, for the investigation of which our methods were fairly adapted and have been successfully applied. To-day, the richest ore lies in deeper levels where the difficulties are much increased and fresh obstacles must be overcome by methods adapted to meet them.

The Degeneration Method, Limitations.—Since the value of information regarding the course of fibers and their relations with cells, derived from the study of degenerations, has been realized, we must attribute to this source nearly every addition that has been made to our knowledge of the anatomy of the tracts of the central nervous system. These methods would serve us equally well and supply us with information of the same value in those regions which still remain unexplored if we could employ them; but their application is made impossible by the nature of the preliminary operations which are required. The same conditions have hampered the study of elementary functions by electrical stimulation, rendering its precise application difficult and depreciating the value of results observed in animals depressed by severe operations and prolonged and deep anæsthesia. So, while advance has been rapid in other directions, ignorance of the functions of the great centers of the brain persists. The largest of them is a silent desert of which our knowledge has advanced scarcely beyond the speculations of Dr. Carpenter of 50 years ago, and for the light which is at length beginning to break upon the functions of the thalamus we are indebted to the refined methods and indefatigable application of recent clinical investigation.

Similar obstacles confront the surgeon and bar his progress. Shock and hæmorrhage, imperfect repair of the protective coverings which are so indispensable, but must needs be destroyed, exfoliations, excrescences, tedious recovery, crippled faculties and a deplorable mortality

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are too often the penalties of an injudicious enterprise upon an entrenched position.

Effects of Exposing Deep Structures.—We watch a trifling intracranial hæmorrhage which does not produce unconsciousness for hours or days and see a patient drift to death or become a helpless cripple and fold our hands, not daring to suggest the scalping knife and tomahawk, and, deprived of our first inspiration and last hope, complacently recommend the expectant attitude while the stream flows by. We cut away the laminæ, expose the cord and divide half a dozen posterior roots on both sides, to purchase a short respite from intolerable neuralgia, which soon recurs, but do not venture to discuss the prospects of section of a tract in the brain. Yet such operations are likely to be available in the future and in practised hands, with a 1 mm. needle and a 5 mm. trephine, may be scarcely more serious than the extraction of a tooth.

Removal of Tumors. Ferrier's Views.—Speaking a few years ago at Bath on the subject of operations for cerebral tumors, Sir David Ferrier[2] said he believed that he was the first to advocate operations on the brain nearly 30 years ago and that he took an active part in the first operation for the removal of a cerebral tumor which was performed by Mr. Godlee. He was perhaps more sanguine then as to the benefits likely to result from the surgical treatment of cerebral tumors, than the experience of the last 27 years had altogether justified. Only a relatively small proportion of cerebral tumors—from 7 to 10 per cent—were amenable to operation, and even this proportion would be reduced if one were to exclude from the operable category the diffuse tumors. The mortality, even in the operable cases, was very great and only a very small proportion of the patients operated upon could be said to have been cured in the sense of having been restored to complete health and usefulness. Desperate diseases, however, required desperate remedies.

The conclusion is not reassuring, indeed it is a counsel of despair for all but those who are satisfied with "desperate remedies" and are able to regard the cure of "only a very small proportion—7 per cent"—as a triumph of surgery. Nor can we encourage ourselves with any definite promise of improvement or hope of advance while we cling to the visual control of intracranial operations with all it entails.

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More Promising Methods.—If our clumsy fingers are to unravel the mysteries or alleviate the disablements of the most exquisite instrument of which our imagination can conceive, it must be by a refined art informed by topographical accuracy not yet approached, aided by instruments whose delicacy and precision will tax our beggarly efforts at construction to their utmost limit, and inspired by a concern for the resources of the victim which will tolerate no scratch, nor jar, nor the waste of a drop of blood that any possible exercise of ingenuity can prevent.

Passing from such anticipations to the practical questions, what is to be the next step? What can we do now? The answer seems to be that the first essential is to ascertain the extent to which we can substitute mechanical direction and control of instruments for the guidance of the visual sense; or, to put it another way, carry out intracranial manipulations without the necessity of mutilating operations, problems of which these pages attempt to offer some sort of solution.

The rigid cranium, which so deeply resents the exposure of the structures it protects, is an admirable base for the direction of fine instruments. It presents landmarks, not perfect indeed, but reasonably satisfactory, supplies fixed points for measurement, and by completely enveloping yielding structures in an immovable frame, gives them a fairly constant relationship to one another and itself, highly favorable to the purpose in view.

Application to Anatomy and Physiology.—The principle of the mechanical direction of instruments on which the methods described here are founded, will probably commend itself so far as it is recognized to be practicable; the extent to which it will be applicable the future must decide, but in some respects its practical value is already assured. For intracranial anatomy, the most minute lesions, or larger ones if required, can be produced in any part of the brain with sufficient accuracy and trifling injury; it thus supplies the indispensable conditions for applying the degeneration method to every part of the brain and enables us to explore tracts and nuclei wherever we wish. The operative advantage may prove equally serviceable to physiology, for though our present methods of electrical stimulation are not capable of affording very much information of the functions of the central ganglia, we may look to the assured progress of electrical science to supply the deficiency and to infuse fresh life into this branch of research.

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Application to Surgery.—In these departments of investigation we have had sufficient experience to speak with confidence of the value of the method, and those who require further evidence can now obtain it in the most satisfactory way by trying it for themselves. But from its application to animals for the objects described to its adaptation to human surgery is a long step, involving, in the first place, a laborious and costly investigation to construct the necessary charts of the human cranium. Possibly, two or three types will have to be represented by different standards, for each of which hundreds of millimeter sections in three dimensions must be cut and photographed. Before this work can be completed an amount of experience will have been collected from experiments on animals which will put the whole subject on a very different footing from that which it now occupies. For my own part, I have no doubt that its application to various purposes in human surgery will be only a question of time, and it will be a source of interest to those who work with the instrument to observe the directions in which the method may be profitably applied to the relief of disease, as well as extended in those fields of research with which it is more immediately concerned.

Physiological Excitation.—As already remarked, the present method of stimulating nerve centers with a faradic current and estimating the effect by muscular contractions is so inadequate for the investigation of central ganglia, owing to escape of current and the fact that many of these centers have no direct connection with a motor mechanism, that improved procedures are greatly needed. Modifications of the current may be found to offer certain advantages, but it is difficult to see how they can ever be entirely free from the same objections.

The stereotaxic instrument may possibly open a more favorable prospect by removing obstacles which have prevented the application to the brain of methods which have given definite results in the cord and nerve trunks. In the experiments recorded by **Gotch and Horsley** in 1891,[4] they found that, by stimulating the limb areas in the cortex of the cat or monkey with faradic currents, they produced very marked negative variations of the electrical current in the cut end of the cord at different levels and in the sciatic nerves. The changes were recorded by a galvanometer and, although slight variations occurred on the same side as the cortical stimulation, they were many times greater on the opposite side, where the impulses were conveyed by the pyramidal fibers following the course of the motor path.

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It is reasonable to expect that similar stimulation of centers in the brain may produce corresponding changes in the course of tracts connected with them; with delicate galvanometers and suitable conductors it may be possible to demonstrate the existence and to measure the rate of transmission of such impulses and the amount of variation produced at different stations in the course of tracts in the brain.

So long as the application of electrodes to precise points in the brain entailed the necessity of exposing the latter by destructive operations, not only was it difficult to direct the electrodes and retain them accurately, but all the conditions were so much affected by the operation that it was hopeless to look for delicate electrical changes, or accept as normal phenomena any results which might be observed. These difficulties are now greatly reduced; we can introduce fine insulated platinum needles through small trephine holes to any required point and keep them securely fixed and connected with galvanometers, under conditions which may be regarded as approximately normal.

The conditions are of course very different from those met within the cord and peripheral nerves. The impossibility of isolating the tract must be a serious difficulty and may be insuperable. But the fact that the galvanometer records changes eight or ten times as great in the path as outside it, even when it is so near as the other half of the cord, encourages the hope that, by means of electrodes applied directly to the channels by which the impulses are conveyed, it may be possible to detect variations in the brain itself. And if such a result can be secured, the information might be so valuable that the subject deserves very careful investigation.

The technique of introducing and fixing insulated platinum needles sheathed in glass, for this or any other purpose, presents little difficulty.

The electrode, preceded by a pilot needle (Pl. XVI, I, 1) which perforates the dura, is introduced through a small trephine hole to the selected point. As the animal will not be kept alive after the experiment, the needle may be secured in position with cement which is softened by heat and hardens rapidly, such as white lead, plaster of Paris, and shellac. Or preferably, two or three thin celluloid discs, rather smaller than the trephine and perforated in the middle, are slipped over the needle before it is introduced; when it is in position each disc is fixed to the needle with a drop of hot shellac and secured in the trephine hole with equal parts of resin and beeswax,

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applied with a brush; this cement is fluid when hot and sets very quickly.

If there is occasion to retain a needle longer, the nickel plugs shown (Pl. XXXV, II) should be used. These are easily sterilized, and nickel is not acted on by the tissues nor does it cause irritation. The plugs were designed to retain fine platinum tubes, 1 mm. in diameter, for draining off serous fluid or for the introduction of minute doses of drugs.

Drugs: Local Action.—It is possible that valuable information may be afforded by the direct action of drugs on brain centers and cells. If we consider the effect of minute doses of prussic acid or aconite introduced into the stomach, and the rapid onset of symptoms, it is obvious that, if the poison acts directly on the cells of the respiratory center, it must pass through the capillaries of the liver and lungs first, and be mixed and diluted with a large quantity of blood. But inasmuch as only a very small quantity of this dilute mixture can finally reach the cells themselves, the amount of the poison which produces the effect must be minute, and the susceptibility of the cells very remarkable. It is worth while making an attempt to ascertain whether any drugs applied directly to central nuclei will produce specific reactions, modify or arrest impulses, or produce changes in the cells themselves which can be recognized; for such results might be of value to the pharmacologist, as well as the physiologist, as a means of testing the properties of these drugs. The platinum tubes referred to are suitable for the introduction of minute doses of powerful drugs and there is no difficulty in dilating the small passage with split cannulæ for tubes of any size for medication, syringing or drainage.

There are one or two other appliances to which I will refer very briefly before proceeding with a systematic description of the instrument.

The varieties of the needle which may be developed in time for all sorts of intracranial operations are practically unlimited. We have made a beginning and illustrations are given of a spherotome (Pl. XVII, IV), designed by Dr. A. T. Mussen, and two or three forms of a cutting needle of mine. The instrument is a hollow steel needle, 1 mm. in diameter, which is just large enough to admit a steel wire and concealed watchspring knife which can be projected and withdrawn as required. In the horizontal cyclotome as seen in the figure

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(Pl. XVI, II), after the needle has been introduced, the knife is projected horizontally from a slot close to the end of the needle. It can be projected any distance up to 4 mm. and a milled head and scale show how far it is extended. The whole needle is then revolved one complete turn, cutting a circular disc from 2 to 9 mm. in diameter, the knife can be retracted, the needle sent in a little further or withdrawn a few millimeters and another disc cut of the same or a different diameter. In this way, circular figures of different kinds, cones, cylinders, barrels of various sizes, can be cut by the introduction of a 1 mm. needle. It is preceded by the pilot needle and the track that is left is quite insignificant; there has generally been no trace of it after the animal has survived for three weeks, and I have not seen any hæmorrhage, except in trephining the bone which sometimes bleeds rather freely, especially in cats.

Section of Tracts.—This form of needle serves admirably for cutting tracts that are parallel to it, the operation being quite simple. In Plate II of the sagittal sections of the cat, in the atlas, the anterior column of the fornix, Vicq d'Azyr's and Meynert's bundles may be seen in sagittal lamella II. If we want to cut Meynert's bundle at the level of the mid-horizontal zero plane, the needle may be introduced in sagittal lamella I or III where they join anterior frontal lamella VIII, *i. e.*, 7.5 mms. in front of the frontal zero plane in the standard. After measuring the head, applying the instrument and exposing the bone by a small incision, the pilot needle is brought over the required point which is marked with ink or a drill, the needle is racked out of the way while a 5 mm. trephine (Pl. XXXV) is applied to this spot, the small disc of bone is removed, and when the bleeding has been checked the pilot needle is brought back and racked down through the dura and brain to the horizontal zero plane. It is removed and replaced by the cyclotome which is introduced to the same point, the knife is projected 1.5 or 2 mm. directly forwards or backwards, the position being known by a line on the milled head, the needle is then rotated through half a circle towards lamella II, the knife is retracted and withdrawn. The tract is found divided by a little incision about 3 mm. long. In the vertical cyclotome (Pl. XVII, VI) the concealed knife is pivoted on its center in the cleft extremity of a hollow needle like the last; when introduced, it lies in this cleft parallel to the needle. It can be rotated on its pivot to a right angle by a steel wire passing down the needle and pivoted near

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the proximal end of the knife, which by this movement cuts two diagonal quadrants. It is then withdrawn by the wire to its original position, the needle is rotated through half a circle, and the knife again projected, cutting the other two quadrants and completing the disc, the plane of which is parallel to the axis of the needle.

In Mussen's spherotome (Pl. XVI, IV) a steel wire ending in a watch-spring knife is introduced into a hollow steel needle, wire, knife and needle being in the same straight line. One side of the needle near the point is filed away to expose a few millimeters of the watch-spring which lies flat, and at its termination is secured by a rivet in a slot close to the end of the needle. When pressure is applied to the wire the spring bulges in the form of a bow, the size and shape of which vary with the pressure applied. By a complete rotation it cuts a spheroidal figure, the size of which depends on that of the knife and the amount of pressure. It will be convenient for the complete resection of nuclei and possibly eventually for breaking up a bloodclot or eviscerating a tumor.

Electrical Resistance, Diagnosis.—The substance of the living brain offers a rather high resistance to the passage of electrical currents. It may be possible to utilize this quality for diagnostic purposes in the case of intracranial hæmorrhage, abscess, cysts and even tumors. If the double platino-iridium insulated needle used for stimulation is included in a circuit with a milliamperemeter, a rheostat and constant battery and introduced with the same current successively into brain substance, muscle and fresh blood, it is generally easy to distinguish them. If the meter records 1 ma. for brain, it will read about 3 ma. for muscle and 8 to 10 for fresh blood. There is some variation due to polarization and also to the condition of the tissues, the amount of fluid they contain, etc., and when blood coagulates its resistance is a good deal raised. Further experiments are required to ascertain how far the results can be depended on.

Kohlrauch's Method.—The above arrangement is a rough one and Kohlrauch's method with an alternating current and coil, a Wheatstone bridge and telephone, is much more delicate and is free from the risk of polarization which cannot be avoided with a constant current. Employing this method, with prepared platinum needles insulated in glass up to their points, which are 1 or 2 mm. apart, I repeated the experiments mentioned with Mr. W. L. Syme in Professor Waller's laboratory and they entirely corroborated the previous

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results. The apparatus gives a direct reading of the resistance in ohms and we tested various tissues and organs as well as brain and blood. The principal results were as follows: Needle points 2 mm. apart and about 2 mm. exposed, platinized black and heated, direct reading:

Saline solution	Resistance	150- 180	ohms
Fresh blood in heart.....	"	300	"
Fresh blood elsewhere.....	"	300- 400	"
Clotted blood	"	400- 500	"
Muscle	"	500- 600	"
Brain *	"	1200-1800	"

The telephone, though very delicate, is not so convenient as a galvanometer where fluctuations of resistance are followed by sight. This is a great advantage not only because it is quicker, but also because the resistance and its variations can be observed while the needle is being slowly racked through the brain. With the telephone, to ascertain the resistance at any point the needle must be stopped and the slide on the Wheatstone bridge adjusted till the telephone is silent when the resistance can be read on the scale. This not only involves more time and trouble, but may be a source of error. Owing to the amount of blood and fluid in the brain a small quantity may collect round the needle when it is stationary and the resistance of the brain appears to be that of the fluid in which the needle is bathed. When the latter is moved on a short distance the resistance increases and the error is detected; and when the needle is kept slowly moving, the accident is not likely to happen. It will, therefore, be an advantage if some graphic method of recording the resistance can be substituted for the telephone. In any case, it seems probable that the method may be of some practical use.

Trephining.—For introducing a needle into the brain a very small trephine about 5 mm. in diameter is sufficient. It should be fitted to a dental engine or a motor and have an adjustable stop. With the ordinary dentist's holder it can be quickly changed. A center pin is only necessary when we require the needle to be exactly in the center of the trephine hole; in that case, the best plan is to use one till a groove is cut and then substitute a trephine with a stop and no center pin. Unless the opening is over a sinus one need not cut the dura. It can be penetrated by the pilot needle, which should be passed down to the

* White matter of brain about 200 ohms higher than grey (cortex).

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required point and then withdrawn, after which the insulated or other needle is passed down the same track. The pilot needle penetrates the brain with less injury than the others; it will perforate membranes if necessary; is not liable to be deflected and should generally be employed.

Arrest of Hæmorrhage.—Hæmorrhage from the small trephine holes may persist for some time and be rather difficult to control without a special appliance. Wax or paraffin are not very satisfactory, as the trephine hole is too small to admit the finger and it is difficult to apply these materials with an instrument to the edge of the diploë, close to the surface of the brain, when the structures are not visible. The effect of the anode in producing rapid coagulation of the blood may be turned to account and an insulated trephine and copper ring will stop the bleeding in two or three minutes, but a self-retaining galvanic plug (Pl. XXXV, I) is more convenient. An overlapping metal collar, rather smaller than the trephine, is fitted over a segmented ivory ring and expanded by a cone drawn outwards by a small screw; when introduced into the trephine hole the collar can be pressed against its circular edge. The plug is connected by an ivory bridge with a hollow copper ring, grooved on its under surface and packed with wool moistened with saline solution. The ring, which is rather larger than the plug, is kept in contact with the bone by the ivory bridge and a small screw exercising counter-pressure against the expanding plug; it is connected with the anode and the metal collar with the cathode, the whole being self-retaining and easy to apply. The leads have been attached previously and directly the crown of bone is removed the plug is introduced and fixed. Three milliamperes are sufficient, but it is advisable to begin with one and increase it. The plug stops the bleeding at once mechanically and, if retained two or three minutes, arrests it altogether. I have had a pair of expanding forceps made for the application of wax or paraffin which may save time and be preferable, in some respects, to a galvanic current.

Many other possible applications of these methods and instruments to cranial surgery will suggest themselves; at present they must be speculative, but some of them are likely to be worth consideration and experiment. Except in a few carefully selected cases, the consensus of present opinion is adverse to the ablation of cerebral tumors by the usual methods and it is improbable that any improvements in technique, on similar lines, will give much more satisfactory results,

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inasmuch as the principal defects are inevitable. If any of the numerous methods of treatment which have been tried or recommended for inoperable tumors should be attended with more success in the future than in the past, the brain is a more favorable region for their application than most parts of the body. Its soft homogeneous structure, insensitiveness, the absence of large vessels and nerve trunks in most of it, its tolerance of small lesions, such as those produced by electrolysis or the passage of needles, the facility with which needles can be directed with the instrument to selected points at measured intervals, are obvious advantages. Numerous punctate or linear electrolytic lesions are well borne and can be very precisely limited. The margins of electrolytic lesions, examined microscopically, are seen to pass abruptly into apparently healthy structure and when a small electrolysis is effected by an insulated needle in an excitable area, if the needle is advanced 2 mm. immediately afterwards and a faradic stimulus applied, it elicits a normal response, showing that the adjacent structures are scarcely affected, even momentarily. Experiment may show the possibility of utilizing such electrolytic lesions to arrest new growths in the brain by cicatricial contraction and it might be expected to have more success in this region than elsewhere, especially if the lesions were produced at measured intervals, representing the nodes of a reticular arrangement enveloping a tumor. The introduction of tubes or needles of radium, the injection of serum or other organic fluids, astringents or alcohol, present no difficulty and what has been said of the possibility of improvement in the diagnosis and, therefore, the treatment of hæmorrhage would be equally applicable to abscess or cysts. The stereotaxic method and instruments are applicable to such purposes and indispensable for most of them. The whole subject offers a promising field for study and investigation.

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CHAPTER II

THE STEREOTAXIC METHOD

Essentials, Topography, Zero Planes and Landmarks, the Horizontal Zero Plane, Correction of Variations of Size, Preparation of Charts and Sections, Proportional Scales

It appeared desirable to begin this description with an explanation of the scope and objects of the stereotaxic method in its more or less evident application to various practical purposes, because, when exhibiting the instrument, the first questions asked me have been, "What is the use of it?" and "What is the advantage of introducing a needle into the brain?" The experimental neurologist does not require to ask those questions, but for everyone the interest of the matter must depend a good deal on the ends he has in view and the probability of their attainment. I have, therefore, endeavored to meet enquiries of that kind at the outset by a superficial and in some respects speculative review of the subject which we must now proceed to examine in detail. The stereotaxic instrument is only part of a method which includes a system of topography and a series of charts without which the machine would be of little value. This has been explained in the first part of the Atlas of Sections which was published in the *Jour. f. Psych. u. Neur.*[5] and which some of my readers may have seen. Others, however, may not have done so, or may have forgotten, and it is so inconvenient to be referred for essential details to some work or paper which is not at hand, that it is advisable to introduce a short explanation sufficient to make subsequent reference to the subject intelligible.

The essentials of the method are:

1. A system of topography by which the cranium can be divided into minute areas which can be readily identified and recorded.

2. The stereotaxic instrument for directing a needle by graduated movement in three planes to any point in the cranium.

3. A series of scale photographs of sections of the frozen cranium, 1 mm. thick, in three planes, to identify and localize any given point so that the instrument can be adjusted accordingly.

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4. A method of correcting variations in size in three dimensions applied to both charts and instruments.

Topography—It is not practicable to make accurate measurements from the irregular curved surface of the cranium, but any point can be localized by rectilinear measurement from central section planes determined by prominent anatomical features. With this object the cranium is divided into eight segments by three sections, each of which is perpendicular to the other two, and approximately median in relation to important structures. They are termed sagittal, frontal and horizontal, and the diameters of the cranium perpendicular to these planes, transverse, longitudinal and vertical, respectively. The eight segments into which the cranium is divided by these sections are described as right and left, frontal, temporal, occipital and cerebellar. The three internal surfaces of each segment are those of a cube, and any point in a segment can be identified by three perpendiculars of correct length dependent from them. Measurements are made from both sides of each section plane which counts as zero.

The position of the section planes is determined as follows:

Section Planes.—A line is drawn from the center of the auditory meatus, determined by a cone, to the lowest point of the lower margin of the orbit on each side. This is the *basal horizontal zero plane.* It is almost entirely below the brain, and to secure the advantage of measurement from both sides another horizontal zero plane is constructed above, but parallel to it. The distance above it is empirical, determined by convenience, and varies with the species of animal employed. In the monkey, it is one-quarter of the distance from the center of the meatus to the vertex, on a line perpendicular to the horizontal plane; in the cat it is one-third and in the hedgehog one-half of this distance, the difference depending on the relation of the interaural line to the brain in different animals. In the above instances the proportions given have the effect of bringing the upper line to something like the same distance, *viz.,* 10 mm. above the meatus with approximately similar relations to the orbits. A frontal section carried down the line referred to from vertex to meatus is the frontal zero plane, while the sagittal zero plane, as already stated, is the median sagittal section of the cranium, determined by transverse measurement through corresponding points on both sides and by well-marked anatomical features.

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Charts. Records and Reference.—The charts are photographs of serial sections of the frozen cranium 1 mm. thick, sawn parallel to each of the three zero planes. In each section, lines representing the other two zero planes are drawn by marks for which the cranium has been drilled before it was fixed in the saw. The slices are called lamellæ, and are numbered from both sides of the zero plane to which they are parallel, the number of a lamella indicating the number of millimeters from the zero plane in the standard. For the purpose of reference the lamella, or the photograph, may be divided into square millimeters by lines parallel to the two zero lines mentioned. The vertical lines (abscissæ) being indicated by numerals, the horizontals (ordinates) by letters of the alphabet. They are counted, like the lamellæ, from both sides of the zero plane. So, by mentioning the segment, the lamella and a letter and number, any cubic millimeter is at once identified and its distance from the three zero planes being conveyed by the same indications, the requisite data are furnished for directing the needle with the stereotaxic instrument.

The above is a short summary of the method of topography of which a description was given in the first part of the Atlas.[5] It is advisable to add some further explanation of a few of the details which have been alluded to, such as the reasons for selecting the present zero planes and adopting two horizontal zeros, corrections for size and proportional scales, and the preparation of charts and microscopic sections. Some of these points will be more fully discussed in another chapter, but a short explanation will meet certain difficulties which may suggest themselves at this stage.

Zero Planes and Landmarks.—With regard to the position of the central zero planes and the anatomical structures by which they may be determined, one, the median sagittal plane, may be considered obvious, being the natural division of the cranium and brain into symmetrical halves. The median plane can be determined by measurement, by bisecting transverse diameters drawn through corresponding points on both sides of the cranium and by various anatomical structures which indicate the median line, sutures, raphés, commissures, etc. These indications generally agree and if there is any discrepancy it is usually slight. When a defect is appreciable, for the localization of a structure, the anatomical guides are to be preferred, as there may be a defect of symmetry evident by measurement of the

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whole transverse diameter of the cranium without affecting the relation of many corresponding points within the brain to the raphé which lies between them. In the selection of the horizontal and frontal zero planes there is room for difference of opinion, and the lines and landmarks most suitable for cranial topography have been thoroughly considered and discussed by anatomists. In some cases, like that of the Frankfort-Munich plane, points selected, *e. g.*, the upper border of the external auditory meatus, may be applicable only to bones or dried preparations and not available for our purpose. Again Chiene's, Grünbaum's and Sherrington's divisions are mainly designed for superficial structures, convolutions and sulci and the meningeal vessels. But what is sometimes called Reid's line from the lowest point of the lower border of the orbit to the center of the external auditory meatus (auricular point), which can be determined accurately in the living subject by a cone, is a well-defined constant and has been adopted as the base line or basi-horizontal zero plane.

Selection of Zero Planes.—It may be objected that a line drawn from the upper margin of the orbit to the center of the meatus corresponds more closely to the base of the brain and is preferable to the one selected. Anatomically it would have advantages and might have been adopted, but there is a practical objection depending on the application of the machine. It is necessary that the frame or head-vice, which is the horizontal zero of the instrument, should coincide with the horizontal zero of the head and, as the machine is too heavy to be supported by the animal's head, it is suspended from horizontal cross-bars, rotating on a central pivot, by four springs which afford complete support without interfering with free movement in every direction, which is essential in stimulation experiments. When the head is fixed so that the present base line coincides with the upper border of the frame and suspended as described, the observer has a good view of the whole face, which is essential, the eyes and mouth being especially important; but if, under the same conditions, the frame is made to coincide with the line from the upper border of the orbit to the meatus a good view of the face is not obtained, a defect with precludes the adoption of this line. On the whole, the lower margin of the orbit appears to be the best level for the basi-horizontal plane and the frame is fixed so that its upper border coincides with it; and as this is the horizontal zero of the instrument from which the scales for vertical measurement are graduated, it

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follows that for directing the movements of the needle for operations and for measuring and comparing the vertical diameters of heads it is most convenient to reckon from this line. But it has also been mentioned that in order to secure the advantage of measuring from both sides of the zero line another horizontal zero which may be called the mid-horizontal, about 10 mm. higher, has been adopted as a standard for general topographical purposes. This appears to introduce needless complication and requires explanation. With the first instrument the mid-horizontal line was adopted as the horizontal zero for all purposes. One of the principal reasons for selecting it was mechanical necessity, as the clamps employed at that time were not very satisfactory and this was the only level where the horizontal frame could be fixed securely, resting on the bridge of the nose with its lower border at the level of the inner canthus bisecting the vertical diameter of the orbit. This may be regarded in a sense as a "natural" position in both the cat and monkey, for if the frame is fixed a little above or below it, unless it is very secure, it works back to this level. With improved clamps the frame can be secured with its upper border level with the base line, bringing the frame about 20 mm. lower in relation to the head than the position in the first machine. There is a decided advantage in the lower level, inasmuch as, the cage and stage being easily removed, the whole head is freely exposed for shaving, trephining, dressing, etc., and the range of the needle is much increased. An objection to making the mid-horizontal line the principal or only zero is the absence of anatomical points to determine it. The inner canthus or the center of the vertical diameter of the orbit may serve for one, but there is nothing posteriorly except a measured distance from the base line or the meatus; and, since the vertical diameters of different heads vary, if the mid-horizontal line is to maintain the same relation to the base line and vertex, as it must, its height above the base must be a constant proportion and not a fixed number of millimeters. For this reason, the proportions of one-quarter of the vertical diameter in the monkey and of one-third in the cat were adopted and after measuring the head the frame had to be adjusted accordingly before it was fixed. In both animals the lower border of the frame came to the level of the inner canthus about 10 mm. above the lower margin of the orbit and the center of the meatus. This level was adopted for measurements of the instrument, for transverse and longitudinal gauging and drilling of the cranium,

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as the horizontal zero plane for segmental division and topography, and for record and reference in notes and descriptions. But the adjustment of the frame after measuring the head required a special mechanism at both orbital and aural attachments which complicated the instrument, wasted time and furnished sufficient reason for adopting the simpler and more satisfactory arrangement now in use.

These considerations appear to suggest the advisability of abolishing the mid-horizontal line altogether and adopting the basi-horizontal line as the horizontal zero for all purposes, but unfortunately there are some for which it is unsuitable. In the first place, it does not serve for longitudinal and transverse measurements of the cranium. It is desirable that these should always be made at the same level through corresponding points; the mid-horizontal plane serves the purpose, although the maximum diameters are a little higher, but the maximum points are not absolutely constant and not much greater than those at the mid-horizontal plane; and if measurements are always made at this level they probably give as trustworthy indications for the estimation of relative size as elsewhere. Again, the basi-horizontal line falls below the greater part of the brain in both the cat and monkey, and if it is employed for segmental division, the advantage of measurement from both sides of it is sacrificed and the cranium is divided into four segments instead of eight. This segmental division is a useful one topographically, especially for affording a method of recording by a short and convenient reference any cubic millimeter in the brain in notes and descriptions and assisting the mental reconstruction which is desirable.

Two Horizontal Zeros for Different Purposes.—A review of the foregoing considerations leads to the conclusion that both the basi-horizontal and mid-horizontal planes have their own special advantages, each one fulfilling certain indispensable requirements which cannot be met by the other, and that the only practicable solution of the difficulty of selecting one of them as the horizontal zero plane is to retain them both, employing them for different purposes. It is essential that the basi-horizontal line, the only one which can be directly defined by precise anatomical landmarks, should coincide with the frame, which is the horizontal zero of the instrument, and thus form a common zero from which vertical measurements for estimating variations of that dimension in different heads are made and the movements of the needle directed. It is equally necessary that a higher level, the

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relative position of which is constant, should be adopted for drilling and gauging in the transverse and longitudinal diameters and for segmental division for topographical purposes and reference, and the mid-horizontal line, as described, is the most suitable for these purposes. The objection that the adoption of two horizontal zeros may lead to confusion, even if well founded, cannot compare in importance with the positive advantages enumerated; and it does not seem probable that when the different objects are clearly recognized, there will be any difficulty in keeping these purposes and the zero planes which serve them distinct and the use of the terms basi-horizontal and mid-horizontal facilitates the distinction. Both lines are shown in the atlas of photographs of sections of the brain of the rhesus monkey prepared by Henderson and myself and published with this description.

Corrections for Variations of Size.—The topographical divisions described would be very simple if the heads of the same species of animal were always the same size in all dimensions, and the chief difficulty encountered is in adjusting the divisions and measurements to the variations in three dimensions which must entail corresponding variations in either (1) the number or (2) the size of the divisions. We can take our choice of these alternatives and there can be no question that the latter is to be preferred. It is important that each lamella should always contain the same structures and that a reference should always mean the same thing; hence, the number of divisions must be constant and their variation in size must be accepted and regulated by the use of proportional scales. If a cranium of average size is adopted as a standard in which the units of measurement are millimeters, when the dimensions are greater or less than in the standard, the units are coordinates bearing the same proportion to millimeters as the whole dimension does to that in the standard; in other words, all heads are reduced to the common measure of the standard for that species in all dimensions and the units of measurement, whether millimeters or coordinates, are regarded as millimeters. This method is followed in the construction of charts. The heads from which the sections are cut vary in size, they are measured and the necessary corrections made to reduce them to the standard in all dimensions. The number of lamellæ in each dimension is always the same, but their thickness is varied by regulating the saw with which they are cut by a proportional scale which is set to measure millimeters or more, or less, as the whole dimension is of standard size, or more, or

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less. The square millimeters, into which every lamella in the standard is divided, are modified in the same way and a corrected scale, proportional to the two dimensions of the selected head represented, is furnished with each photograph and employed, instead of millimeter scales, to measure the distance of any point in the section from the zero lines. After the selected head has been measured, before it is removed from the gauging and drilling cage, the position of the zero plane is marked on the surface and the cranium is drilled at three points perpendicular to the plane of the proposed sections. One puncture is at the intersection of the two perpendicular planes and the other two 10 mm. on each side of it in one of these planes. The punctures of the drill appear as dots in every section and with their help the crossed lines representing the zero planes perpendicular to it can be defined. A needle is left in the central puncture and is used to adjust the head accurately in the vice of the saw. Heads are kept till sufficiently stained and hardened in formalin 5 per cent and potassium bichromate 2 per cent. They are then frozen in carbonic acid snow and adjusted in the vice of the saw; the scale of the saw, which is composed of silk threads, is set in accordance with the measurements of the dimension to be cut, the intervals being actually or approximately 2 mm. With the saws now used little more than .5 mm. is destroyed by each saw cut and the slices are therefore nearly 1.5 mm. thick. Each slice represents two lamellæ and both surfaces are photographed. Scales are prepared corresponding to the diameters of the crossed zero lines and attached to the photographs.

Microscopic Sections.—It is an advantage, especially for students, to carry out the same topograhical methods in the preparation of microscopic sections, for in this way the localization and description of lesions and degeneration are facilitated. Sections should be cut parallel to one of the zero planes and the division into the standard number of lamellæ for each dimension maintained. The procedure is described in Chapter VI.

References and Records.—It has been mentioned that any cubic millimeter in the brain can be identified and recorded by a simple formula giving the segment, lamella and the number of millimeters, or coordinates, between the given point and the zero lines of the lamella. To distinguish the latter, letters of the alphabet may be employed for the vertical units and numerals for the horizontal. This is applicable only to sagittal and frontal lamellæ. If they are hori-

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zontal, the zero plane must be distinguished by a letter *T* or *L*, for transverse or longitudinal. But as it is very easy to transpose the indications for one dimension to another, it is best to make all references in the sagittal plane and, if that is understood, the word sagittal may be omitted. Left frontal segment, (sagittal) lamella VI, b4, indicates a cubic millimeter, 6 mm. to the left of the sagittal, 2 mm. above the mid-horizontal and 4 mm. in front of the frontal zero planes, respectively. As comparatively high numbers and still more late letters of the alphabet are more difficult to follow than the earlier ones it may be convenient, when high numbers are involved, to divide the surface of each lamella into 5 mm. squares, called divisions or blocks, distinguishing the vertical ones by capital letters and the longitudinal by Roman numbers, the small letters and the ordinary numerals being still retained for single millimeters or coordinates. Thus *Dc* would represent 23 mm. or coordinates vertically and III 2, 17 mm. longitudinally.

Proportional Scales.—Two kinds of proportional scale are employed and fully described in a later chapter. The most accurate form is constructed of parallel silk threads stretched between equidistant pegs arranged on opposed sway bars, the inclination of which approximates all the threads and diminishes the spaces between them equally. It is perfectly accurate, although not always applicable, but is employed with the saw and with the indicator, which will be described presently. In the rectilinear machine, however, where the movements of the needle in three dimensions are directed by scales attached to the instrument this form would be too cumbersome, and a proportional scale (pl. IX) is employed, consisting of a spiral spring enclosed in a tube, one side of which is cut away to expose the spring, whose spirals are units of measurement. When relaxed, the spirals are rather less than 1 mm. apart; by a slight extension of the spring, which can be fixed anywhere, the spaces measure millimeters or more, and with a little care in adjustment are sufficiently accurate though not equal to the silk threads. However, for the purpose required, an error of a small fraction of a single millimeter is not important, but a cumulative error which may sum up in a whole dimension to several millimeters is serious and such a risk is completely prevented by the spring scales.

Gauging of Cranium.—The first proceeding in an operation on a selected animal is to apply the gauging and drilling cage and take

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the measurement of each dimension, from the central zero plane to the parallel surface of the bone, with the needle gauge. The points of measurement correspond to the three zero planes; the dimension recorded being perpendicular to one and parallel to the other two and taken at the point of intersection of the latter. The measurement of each dimension is compared with the standard and the proportional scale used for that dimension is set accordingly. The number of divisions of the proportional scale is, therefore, the same as in the scales of the chart and both are regarded as millimeters, although in reality neither of them may be millimeters and they may not measure the same. But they are treated as identical and all movements of the needle and measurements of selected points regulated by them, the result being the same as if all the heads selected were of standard size in all dimensions and the units of measurement were millimeters.

The following are the dimensions of the standard cranium of the rhesus which have been adopted in accordance with the method for the chart sections of the atlas for which all measurements were made with the needle gauge in the special cage shown in Plate XXXIV.

Longitudinal diameter: Prefrontal, 50 mm. Postfrontal, 30 mm. Total, 80 mm.

Transverse diameter: Right half, 30 mm. Left half, 30 mm. Total, 60 mm.

Vertical diameter: Supra-horizontal, 30 mm. Sub-horizontal, 10 mm. Total, 40 mm.

Longitudinally the prefrontal dimension extends in the median sagittal line from the frontal zero plane to the glabella. The postfrontal from the same zero plane to the occipital protuberance (inion).

Transversely each half is measured laterally from the sagittal zero plane to the point of intersection of the frontal and mid-horizontal zero planes on the surface of the cranium.

Vertically, the lower quarter extends from the mid-horizontal zero plane to the interaural line; the upper three-quarters, from the same zero plane to the point of intersection of the sagittal and frontal zero planes on the vertex.

The figures given are very near the average of a large number of heads that have been measured and are fortunately very convenient numbers for comparison.

In the paper in *Brain* previously referred to[1] the average dimensions of 32 heads of the rhesus were given. They differ slightly from

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the above, but the discrepancy is very slight and is due to improved methods of measurement which are now adopted. If the two sets of figures are compared, it will be seen that in the vertical diameter they are the same. The total longitudinal diameter is 80 mm. in both, but differently divided; in the paper, the prefrontal and postfrontal divisions are given as 47 and 33 mm. instead of 50 and 30 mm. as above; and the transverse measurement is 32 mm. on each side or 64 mm. altogether instead of 60, a difference of 4 mm. in the whole dimension. The explanation is that in the first place the measurements in *Brain* were made with calipers and included the skin, and secondly they represented the maximum transverse diameter, whereas now they are always taken with the needle gauge to the surface of the bone and between the same points, *viz.*, the intersection of the frontal and mid-horizontal zero planes on each side, and this is generally not quite the maximum diameter as already explained.

The difference in the longitudinal measurement is also due to an improved method. Formerly it was made with calipers from the anterior termination of the mid-horizontal line a little below the nasion to the inion, including the integuments, which in the latter region are rather thick. The needle gauge, penetrating to the bone, makes the posterior measurement from the frontal zero plane to the inion rather less; but in front, measuring in a cage between perpendiculars, we consider the glabella, which is the most prominent point of the cranium, the best feature for the purpose. The result is that the anterior longitudinal dimension is rather more, the posterior rather less than the former estimate, but the total diameter is the same.

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CHAPTER III

STEREOTAXIC INSTRUMENTS

Directing Mechanism, General Description, Principles and Requirements

Principles.—We have now to consider the mechanical direction of some form of needle or fine instrument to any desired point in the cranium. The position of the three zero planes and the method of determining and expressing their relation to any point have been explained and the principle of the required mechanism may be defined by a few self-evident propositions:

1. If we know the distance of a given point in the cranium from each of the three zero planes and can direct a needle to any required distance from these planes, we can direct it to the given point.

2. There is no mechanical difficulty in constructing a needle-carrier fitted to rectilinear traversing guides, or to an equatorial, like that used with an astronomical telescope, either arrangement being so disposed in relation to three central, mutually intersecting planes, each of which is at right-angles to the other two, that, within the limits of its excursion, the needle can be directed by graduated movements to any point of known distance from the three planes.

3. If we fix the head in such a structure so that the three zero planes of the cranium and instrument coincide, the needle can be directed to any point in the cranium of known distance from its three zero planes.

Requirements.—Assuming the accuracy of these principles, the next consideration is the most suitable instrument to give them effect. As with most mechanical contrivances, we are confronted with various practical difficulties, the solution of which is often a compromise, advantages in the one direction being purchased by sacrifice in another; and the most efficient instrument may not be worth its cost, compared with a cheaper one. The instruments here described have been evolved by attempts to solve these problems and, as far as they go, are a practical answer to questions respecting the nature and relative importance of the principal requirements, of which the following may be enu-

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merated: Accuracy of adjustment and measurement; scales which register the position of the needle, or similar instruments, in all circumstances without involving calculation; speed and simplicity; adequate rigidity; provisions for introducing and changing various forms of needles for cutting, electrolysis, or faradic stimulation and arrangements for correcting variations of size of different heads in three dimensions; electrical connections are also necessary for directing constant or faradic currents through the needle by different routes. In the descriptions and illustrations the reader will recognize the purpose of numerous contrivances, draw his own conclusions as to their adequacy and perhaps see his way to improvements.

Present Instrument: Two Patterns.—Three stages may be noted in the development of the instrument in its present form. In the first, the movements of the needle are entirely rectilinear and are measured directly by millimeter scales engraved on the guides of the machine or attached to them. The next step was to supplement the rectilinear movements and give a greater range to the needle, by providing for its inclination at various angles, but only in one plane and in one direction in each position, of which there are seven. These inclined movements are measured and regulated and the corrections for size effected by an indicator of either two or three dimensions; while in the latest pattern universal movements of the needle, from any position, are secured by fitting it to a form of equatorial and all movements and corrections for size are determined by a three-dimensioned indicator. The range and flexibility of the needle have been much extended and the utility of the instrument increased by the introduction of indicators of two or of three dimensions; they will be fully described and illustrated in their place, but some account of them will be given in this chapter. Direct measurement of inclined or universal movements of the needle, out of sight, and with necessary corrections for variations in the size of different heads, was not found practicable, but a satisfactory alternative is obtained by reproducing an exact representation of the mechanism by which the needle is directed to an objective in the cranium, at a given distance from its three zero planes in another instrument, the indicator, where the structures are visible and the needle can be guided by sight to an index point at the same distance from three coincident index planes and the movements repeated by corresponding scales in the machine which contains the head. This method has great advantages, but for simple

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rectilinear movements a cheaper instrument can be employed. For such movements no indicator is required, the rectilinear machine is sufficient and is much less expensive than the complete instrument with equatorial and indicator. This machine cannot therefore be considered obsolete and I propose to give here a short general account of it and the methods of measurement adopted, followed by a similar description of the inclined needle adapted to this machine and the two-dimensioned indicator by which its movements can be regulated, and finally, of the equatorial and three-dimensioned indicator. This description will supplement and not supersede the detailed account of all the instruments which will follow and, although it involves a certain amount of repetition, it will make the subject more intelligible to begin with such a general survey. The complete descriptions of all the instruments which it is necessary to introduce contain a number of details which it is tedious and confusing to follow before their objects and mutual relations are recognized, but if the reader obtains a general impression of the nature and objects of the various instruments and the method of using them, he can then follow the detailed descriptions as far as he pleases.

Frequent reference has been made to corrections for size, which is an indispensable consideration with any form of instrument, and as the problems it raises and the provisions for solving them must be frequently encountered, it will be convenient to discuss them first.

Corrections for Size.—If the heads of animals of the same species were all the same size, the application of the foregoing principles would be simple. We need only prepare a series of charts of the cranium of the selected species, from sections 1 mm. thick, in one or more planes, photographed to scale, with crossed lines indicating the other two zero planes in each chart, to enable the operator to ascertain the distance of any point from the three zero planes and direct the needle by those measurements to reach the same point in the head, already adjusted and fixed in the machine. But as variations, in any dimensions, of selected heads are to be expected and may be considerable, a method of correction is indispensable and the following has been adopted.

A standard head of approximately average dimensions is assumed and divided by imaginary sections, parallel to the zero planes, into cubic millimeters, each slice or lamella being 1 mm. thick and sub-

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divided into square millimeters. By these divisions or ordinates the distance of any point from the zero planes can be readily ascertained.

Charts.—This theoretical standard is represented by charts, which are scale photographs of sections of the frozen cranium, in one or more planes, cut with a special saw, described in the first part of the atlas. Since it is very difficult to find heads of exactly standard dimensions, while the number of lamellæ and their subdivisions must be constant, the size of all subdivisions must vary proportionally to corresponding dimensions of the head. This is effected by proportional scales. As the heads selected for charts may be larger or smaller than the standard, the lamellæ may be more, or less, than 1 mm. thick and the square millimeters or coordinates, into which they are divided, may measure more or less than 1 mm. in either dimension. The head to be sawn is measured with the needle gauge (26) in the measuring cage (Pl. XXXIV), the result in millimeters is noted for each dimension and compared with the standard and the proportional scales are set accordingly. The scale now used with the saw for regulating the thickness of the lamellæ is a grating of parallel silk threads stretched between opposing sway bars. The threads are approximated by inclining the bars and can be set at intervals of 1 mm. or more, or less, by direct measurement, or by quadrant scales with which the grating is provided; the spaces between the threads being the coordinates which determine the thickness of the lamellæ cut by the saw. A reticulated screen is formed by two such gratings, one being superimposed upon the other, at right-angles to it; when the intervals in both gratings are equal, the meshes form squares, but as the gratings can be adjusted independently, the meshes may measure millimeters, or more, or less, in either dimension. The subdivisions of the lamellæ are regulated by this screen; in the standard they are square millimeters; in the selected head, the same number of divisions are made to measure millimeters, or more, or less, in either direction as the whole dimensions measure the same as the standard, or more, or less.

The **corrected screens** serve as scales of measurement which are photographed with the lamellæ, bringing them in both dimensions to the common measure of the standard head. This is the method of preparing standard photographs or charts.

Measurement of Heads.—The heads selected for operation must be measured and their dimensions compared with the standard in a similar way. If desired, millimeter scales may be used for directing

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the needle, the necessary corrections for each movement in three dimensions being made by calculation or tables. It will be found in practice that when a number of observations are required, as in stimulation experiments, such constant interruptions as this involves are irksome and a mechanical method which effects the correction automatically is preferable. Two methods of this kind have been employed. For simple rectilinear movements a form of extensible scale (Pl. IX) is used which consists of a small steel spring enclosed in a tube with a longitudinal slot to expose the spring, the spirals of which serve as divisions of the scale. When the spring is slightly extended, the spirals are 1 mm. apart; they can be fixed at any point and made to measure millimeters, or more, or less. The rectilinear machine is provided with three of these scales to direct the excursion of the needle in three planes, and for this purpose they are regarded as ordinary millimeter scales; with a little care in setting them they are sufficiently accurate.

Adjustable Gratings.—The gratings of silk threads, already mentioned, are employed with the same machine, in a two-dimensioned indicator (Pl. XXVI) to direct the movements of the inclined needle, and three such screens are combined in a three-dimensioned indicator (Pl. XXVII) in the later modification. These gratings are the most satisfactory form of proportional scale; they are perfectly accurate and quickly adjusted. The three-dimensioned indicator is used to direct the movements of an operating instrument constructed on the principle of an equatorial, which gives the needle universal movement, an obvious advantage. Thus, by measurement from central zero planes with proportional scales, all heads, whether used for charts or operations, are reduced to the common measure of the standard head in all dimensions and the coordinates which form the units of measurement are equivalents of millimeters in the standard and are regarded as identical.

Having now given a summary of the principles on which the stereotaxic method is founded, a sketch of the use of charts, their preparation, corrections for size, measurement by proportional scales and the application of the same means to correct variations in the dimensions of heads selected for operation, I propose to complete this chapter with a brief review of the procedure adopted to direct and measure the movements of the needle in the two patterns of machine, including the two forms of indicator which have been mentioned.

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Operating Mechanism. Direction and Measurement of Movements

A selected animal having been prepared and anæsthetized, the first step is to measure the head in three dimensions with a needle gauge, which gives the cranial measurements free from errors due to variations in the thickness of integuments, hair and muscles. With the rectilinear machine a needle gauge (Pl. XXIV) may be used with a rectangular cubical skeleton table, the cage (Pl. X, 64) attached to the head by the basal frame or head-vice (Pl. V). This is a quadrilateral, horizontal frame which surrounds the head at the level (22-23) of the basal plane and is fixed to it by two pairs of graduated screw clamps. By a pair of aural pivots (25) and orbital brackets (Pl. II, 9) secured by a face-piece or mask (Pl. II) and bit (8), the upper border of the frame is made to coincide with the center of the meatus and the lower border of the orbit on both sides, *i. e.*, the basal zero plane, and it is clamped in this position. At the same time, as the clamps and aural pivots are graduated and made to correspond on both sides, the head is centered, so that the median longitudinal plane of the frame coincides with the median sagittal plane of the head. The basal and sagittal zero planes of the frame and head therefore coincide and the frontal zero plane is also identical in both as it is drawn through the centers of the aural pivots and auditory meatus at right-angles to the line from the center of the meatus to the lowest point of the orbit, *i. e.*, the upper border of the basal frame. The basal frame or head-vice and the method of applying it are identical, whichever operating instrument is subsequently employed, and with both measurements are made with a needle gauge applied to a cage, but the latter is constructed in two forms. The cage (Pl. X, 64) is an essential part of the rectilinear instrument. The traversing stage (Pl. XIII) and needle carrier (71) are applied to its free surfaces and these also serve as bases for the needle gauge which is merely a form of depth gauge (Pl. XXII). But in the later machine, for operative purposes, the equatorial (Pl. XXX) takes the place of the cage, which is then required only for measurement with the needle gauge, and it is therefore advisable in this case to employ a cage constructed solely for gauging and drilling (Pl. XXXIV). The drill may not be wanted, but as the same guides serve for both gauging and drilling, the additional cost of it is trifling, and it is an advantage that it should be

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available, if required. The objects for which it is necessary are explained in Chapter V. It is sufficient to mention here that with the rectilinear machine the ordinary cage is employed; the measurements in all available dimensions are taken with the needle gauge (Pl. XXII), and then the traversing stage (Pl. XIII) carrying the operating needle is applied to the same cage. If, however, the equatorial be used, a special measuring and drilling cage (Pl. XXXIV), which includes a needle gauge (26), is employed for measurement only, then removed and the equatorial substituted. Both forms of cage are furnished with four similar feet (Pl. X, 67-68) carrying bolts which fit into slots in the head-vice (Pl. V, 42-43) and are then locked.

Adjustment of Spring Scales.—In the rectilinear machine, after the selected cranium has been measured and the three adjustable spring scales (Pl. IX) have been set in accordance with its dimensions, their divisions will have the same proportion to millimeters as the whole dimensions of the selected head have to the standard, and the needle is directed by these coordinates instead of millimeters. The next step is the application to the cage (Pl. X, 64) of the traversing stage (Pl. X, 69) which carries the needle.

The Traversing Stage.— The needle carrier (Pl. XIII, 71) is mounted on a quadrilateral, rectangular frame (Pl. XIII, 69), like a microscope stage, with rack and pinion movements in both directions. The carrier (71) consists of a slide block travelling on the transverse guides of the stage (70 *a*, 70 *b*). Attached to this block, perpendicular to the stage, is a grooved plate, the outer sheath (Pl. XIII, 72), in which the inner sheath (Pl. XIV, 93) of the needle-holder slides. The outer sheath is attached to the slide block by a pivot and quadrant (Pls. X, XI, XII, 77) providing an inclination of 25° in one plane and direction, and the bed of the needle (Pl. XIV, 94) can be projected from the inner sheath by rack and pinion, completing the graduated movements of the operating needle in three planes.

The excursions are registered by millimeter scales to which extensible spring scales are fitted and both are read simultaneously by the same index. By means of steady pins and clamps the stage can be fixed to any of the free surfaces of the cage, above (Pl. X) where it can be made to face four different ways, to both sides (Pl. XI) and behind (Pl. XII), seven positions in all. When fixed in any of these positions the zero points of its scales coincide with the zero planes of

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the head-vice and cranium and the engraved millimeter scales of the guides of the stage are graduated from both sides of these zero points.

Direction of Movements of Needle.—Whatever the position in which the stage is fixed, the index of the needle (Pl. XIV, 113) reads zero on its scale (Pl. XIV, 112) when the point of the needle reaches the zero plane of the cranium to which it is perpendicular, and however the needle is racked in or out, its index always shows the number of millimeters on the millimeter scale (112) and coordinates on the extensible spring scale (111) from the point of the needle to that zero plane. Similarly, the scales of the stage (Pl. XIII, 70-91) show the number of millimeters and coordinates between their zeros and the needle, and as these zeros coincide with the zero planes of the frame and head, we can recognize immediately how many millimeters and how many coordinates the needle is from the three zero planes of the cranium. The method of directing the needle to a given point in the brain by this mechanism can be made more intelligible by an example.

Localization of Objective Point.—Since any objective point in the brain must be found, in one lamella at least, in each plane, we may take our choice and locate it in the plane which appears most convenient in practice or, as in this case, merely to serve as an illustration. Let us assume that the needle is to be directed transversely from one side (Pl. XX), that the objective is a point in the thalamus, and that we decide to locate it in a sagittal lamella perpendicular to the needle, the number of the lamella corresponding to the number of millimeters or coordinates from the objective to the median sagittal plane. In the chart of the selected lamella we measure the distance of the objective from the lines representing the basal and frontal zero planes, using the corrected scales of the chart and regarding the units as millimeters in the standard. These are the data. We proceed to rack the needle the same number of coordinates on the extensible scales of the stage from the zeros coinciding with the basal and frontal zero planes by the two movements of the traversing stage which is parallel to the sagittal lamella and thus bring the needle exactly opposite the objective, pointing at it. The third movement, the projection of the needle in its sheaths, will bring it to the required point. To any one familiar with the instrument, it does not matter which plane is selected to locate the objective. If we located it in a frontal or horizontal lamella, parallel to the axis of the needle, we should bring

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the latter to the edge of the lamella with one movement of the stage, and the other movement of the stage and the projection of the needle would bring the latter to any desired point in the lamella.

The Inclined Needle.—The outer sheath of the needle carrier (Pl. XIII, 72) is pivoted and swings on a graduated quadrant (77) which provides for an inclination of about 25°, within that limit it can be fixed at any angle in one direction and in one plane, but it can be applied to the top of the cage facing four different ways and therefore inclined in four directions, and by the movements of the stage it can be brought to any lamella in any plane, and thus the angular deflection is available, if required, in many positions. The inclination being only in one plane, the objective must be located in a lamella parallel to it and therefore perpendicular to the stage. By one movement of the stage we bring the needle to the edge of the lamella, set it at the required angle, and then, by two remaining movements, one of the stage and the other the extension of the needle in its sheaths, we can direct it to any point in the lamella. As an example, let us assume that we propose to direct the needle, from above, to a point in the right internal capsule, avoiding the caudate and lenticular nuclei. We locate the objective in a frontal lamella, fix the stage, above the cage; with the needle facing forwards (Pl. XIX) its plane of inclination will be parallel to the lamella and deflect the point of the needle to the left, the direction of the right internal capsule; the needle is set at the same angle as the capsule and fixed by the quadrant. We have employed one movement of the stage (longitudinal), measured by its proportional scale, to bring the needle to the edge of the lamella; there remain the transverse movement of the stage and the projection of the needle, and with these two movements it would be easy to direct the point of the needle to the objective if both were visible. This is not possible in the head, but we can reproduce the conditions in an instrument where we can see them, direct the needle to the required point by sight and by means of corresponding scales repeat the movement in the operating mechanism.

Two-Dimensioned Indicator, with Card.—Such an instrument is called an indicator. In the proposed example it need only be of two dimensions, for the needle has been brought to the plane of the lamella and we only want to ascertain the extent of the two remaining movements required to bring it, at a given angle, to the desired point. This can be effected by representing the lamella by a card ruled with square

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millimeters and crossed by two lines corresponding to those marking the zero planes in the charts. If we remove the head and fix the card in the machine in exactly the same position as the lamella, so that their crossed zero lines coincide, the needle, fixed in any position, must have the same relations to those lines, and to any points at the same distance from them, in both card and lamella. We may therefore mark a square millimeter on the card, a given number of millimeters from the crossed lines, bring the point of the needle into contact with it, note the position of the needle by its scales, then retract it and replace the head in the machine and finally project the needle again to the position noted on the scale, to bring it to a point at the same distance from the two zero lines of the lamella in the brain as the square millimeter on the card is from its crossed lines. We can begin this proceeding by fixing the needle at a given angle on its quadrant scale and bring it to the marked square by two movements, one of the stage, the other its own projection, and by identical movements bring it to the objective point in the lamella, inclined at any required angle within the limits of its excursion. To save the trouble of removing the head from the machine and replacing it, the card may be fixed in a duplicate machine, the needle directed by sight to the marked square, and then by corresponding scales the movements can be repeated in the operating instrument and its needle brought to the objective point in the brain. It is not necessary that all the details of the operating machine should be reproduced in the duplicate if we secure the representation of those which are essential. The first step, when using the inclined needle in the operating machine, is to bring the needle to the edge of the selected lamella by one movement of the stage; this eliminates one dimension in the localization of the objective, the remaining movements, one of the stage, the other the projection of the needle, as well as its inclination, are in the plane of the lamella, so the duplicate instrument or indicator only requires two dimensions and the essentials of the operating mechanism are represented by a ruled card enclosed in a square frame, one side of which serves as a guide for a slide block on which an extensible needle or finder is pivoted with a quadrant and scale to fix it at any angle. The details correspond exactly with their counterparts in the operating machine; the size is the same or proportional throughout, and all scales are identical, so that movements in one instrument can be repeated in the other. As the card and the scales are graduated in millimeters, the measure-

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ments are applicable only to heads of standard size; variations in the two dimensions represented of any selected head must be corrected by calculation, or by substituting for the ruled card an adjustable, reticulated screen formed by two superimposed gratings of silk threads at right-angles to one another (Pl. XXVI). The screen is adjusted to correspond with the two dimensions of the lamella of the selected head, the meshes are then coordinates representing the square millimeters of the card and the index point is determined, by counting them in the same way, from the central threads of the gratings which represent the crossed zero lines.

The Three-Dimensioned Indicator and Equatorial.—So far the description applies to the rectilinear machine with a single inclined movement of the needle and the method of directing it with a two-dimensioned indicator. It will be evident that considerable advantages may be secured by mounting the needle on an equatorial (Pls. XXIX-XXX), which affords universal movement, and directing it entirely by a three-dimensioned indicator (Pl. XXVII). These instruments are fully described in their place (Chapter VI), but with the help of the illustrations a short explanation will be sufficient to give the reader a general idea of the mechanism and its application, which is all I propose to attempt in this chapter. The equatorial is used as a substitute for the cage and stage of the rectilinear machine, the needle is carried in much the same way as the telescope in the astronomical instrument and has practically universal movement. The equatorial is supported on four feet terminating in bolts like those of the cage and they fit into the same slots in the head-vice; when applied to the indicator they fit into corresponding slots which have the same relations to screens representing the zero planes as the slots in the head-vice have to the zero planes of the cranium. Thus, the same equatorial can be adjusted in the indicator and the needle directed to the index point by sight, then transferred to the head-vice, and the needle will reach an objective with the same relations to zero planes of the cranium as the index has to the zero planes or index planes in the indicator. This method has the advantage of the greatest possible simplicity, for, though all the movements of the equatorial are recorded by scales, when it is used in this way, none of them need be employed except that which registers the projection of the needle. Obviously, the needle must be retracted while the skull is trephined and then

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racked in till it reaches the figure noted on the scale, when it will be at the objective point. On the other hand, if duplicate instruments are employed, one applied to the indicator and the other to the head, a comparatively complicated operation can be carried out in the indicator and repeated step by step in the operating machine. In this case, every movement of both equatorials is regulated by the scales and precisely copied.

Three-Dimensioned Indicator with Ruled Card.—The simplest form of three-dimensioned indicator is a modification of that already described with a ruled card; it is provided with a horizontal table carrying a card ruled with square millimeters and crossed by two lines, representing the frontal and sagittal zero planes, like the chart of a horizontal lamella; the position of these lines being fixed in constant relation to four pillars with slots which correspond to those of the head-vice, so that the needle must have identical relations to the zero lines in both cases. The table carrying the card is supported on an extensible vertical pillar, graduated with a millimeter scale, by which the table can be raised or lowered with a rack and pinion. The upper surfaces of the slots of the four pillars represent the basal zero plane, as it does in the head-vice; and when the table is at this level the scale on the pillar is marked zero; the table can thus be raised or lowered any required number of millimeters above or below the basal plane. The index point is measured the same number of millimeters from the crossed zero lines on the ruled card as the objective point is from the corresponding lines on the chart of a horizontal lamella, and the square millimeter on the card is marked; the table is then racked to the correct height in relation to the basal plane and the marked square will be at the required distance from the three zero planes. The equatorial or cage can now be applied to the slots in the indicator and fixed, the operating needle directed from any position to the marked square on the card, the scale of the needle noted and the needle retracted sufficiently to be out of the way. Then, the equatorial, or cage, is transferred to the head-vice, the needle racked in till it touches the skull, this point is marked and the equatorial removed while the skull is trephined, then replaced and the needle racked through the brain till it reaches the objective point. As in the two-dimensioned indicator, this method with a ruled card has the disadvantage that there is no provision for correction for size and it is

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necessary to make any that is required by calculation or tables. It is therefore more satisfactory to use the gratings in three dimensions.*

Three-Dimensioned Indicator with Adjustable Gratings.—(Pl. XXVII *et seq.*) Two horizontal gratings, one applied closely above the other and at right-angles to it, form a reticulated screen, the meshes of which can be made to measure millimeters, or more, or less, in both dimensions. To facilitate counting the threads they are divided into groups of five by contrast colors; white threads extend between the opposed pivots of the sway bars in each grating and represent the zero planes; other white threads are introduced to show the transverse and longitudinal dimensions in the standard cranium of the cat and monkey. One of the gratings is longitudinal, its central white thread represents the sagittal zero plane, and the intervals between the threads are the coordinates of transverse measurement. In the grating at right-angles to this the intervals are units of longitudinal measurement and the central white thread the frontal zero plane or interaural line. Vertical measurements are provided for by a single gridiron grating fixed vertically like a lawn-tennis net. A white thread between the pivots of its opposed sway-bars represents the basal zero and is level with the upper surface of the slots. All three gratings are set by direct measurement or quadrant scales, with which they are furnished, to correspond with the three dimensions of the selected head, or any segment of it.

An index point representing the objective point in the brain is adjusted in relation to the three gratings; it may be represented in several ways, the simplest of which is shown in Plate XXVIII. A vertical index needle (24), which can be raised or lowered in a slot at the end of a horizontal radius bar (23) by which it can be brought over any mesh in the reticulated horizontal screen, is fixed at any required distance from the sagittal and frontal zero planes and represents the index point in two dimensions. A horizontal index needle (29), carried in a vertical radius bar (27), is made to correspond with the space representing the required height above or below the basal plane in the vertical grating (16) and provides the measurement in

* The introduction of the card was suggested by Mr. Vellacott on grounds of economy. I have not employed it, as I think the correction of measurement by calculation, which it entails, is objectionable; the card is, however, much cheaper than the adjustable gratings and on this ground the method may be worth consideration.

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the third dimension. If the points of the two index needles are made to meet, as shown in Plate XXVIII, either of them will serve to indicate the position of the index point, and the operating needle can be directed to it and, one index needle having been selected, the other may be removed. In practice it is rather inconvenient to bring the points of two needles precisely together like this; if the needles terminate in notches instead of points or one of them in a cross (Chap. IV, XXVIII, A), they can be adjusted more quickly. The operating needle of the equatorial or cage is directed to the index point, as explained in the description of the card indicator, and the subsequent steps of the operation are completed in the same way.

PLATES I TO XXI

Plate I.—Ear cones, guide, speculum, probe.

Plates II, III.—Mask.

Plates IV–VIII.—Horizontal frame or head-vice.

Plate IX.—Extensible scales.

Plate X.—The cage and needle, first position.

Plate XI.—The whole rectilinear machine with inclined needle, applied to cage in sixth position.

Plate XII.—Horizontal needle applied to rear face of cage, seventh position.

Plate XIII.—The traversing stage.

Plate XIV.—The needle-holder.

Plate XV.—Insulated platino-iridium needles.

Plates XVI, XVII.—Operating needles and beds.

Plates XVIII, XIX, XX, XXI.—Needle and stage applied to cat's head fixed in cage and head-vice. Needle in same position as in Plates X, XI, XII, in which the parts of the machine are numbered. The numbers are not repeated in Plates XVIII–XXI.

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CHAPTER IV

ILLUSTRATED DESCRIPTION OF STEREOTAXIC INSTRUMENTS

PLATE I

(IV) Ear cones for cat. (III) Ear speculum for cat. (I) Guide and (II) Probe for introducing cones.

(IV) These are hollow brass cones introduced into the auditory meatuses on both sides. The external orifices receive the tapered ends of the aural pivots (Pl. V, 25) which are fixed in the frame or head-vice (Pl. V). Their object is to support the head in the correct position in the frame till the screw clamps are adjusted and fixed. The cones center the meatus and, when fitted on the aural pivots, the interaural line, which passes from the center of one meatus to the other, is on a level with the upper surface of the head-vice which coincides with the basal horizontal zero plane of the cranium. Both cones and pivots are bored so that in the cadaver the interaural line can be drilled from one pivot to the other.

The meatus in the cat is not very accessible and, as the accuracy of the interaural line is the most important of all the data for adjustment and measurement, various forms of ear cones have been tried. The simple straight cone with only a slightly projecting disc is the best. It consists of the following parts: (1) The point or cone; (2) The disc; (3) The barrel. The point enters the meatus, the disc prevents it from going too far and the barrel receives the pivot. The introduction of the cones will be discussed under the head of operative procedure and will be referred to here only so far as may be necessary for the description of the instruments illustrated in Plate I, *i. e.*, the speculum and guide. The former does not require description. Its use is to expose the orifice of the meatus and when introduced for this purpose the pinna should be drawn directly outwards and illuminated with a good light. In the cat the orifice of the meatus is generally a mere slit and may be invaginated by the blunt point of the cone; it is sometimes advisable to use a guide to introduce the cones and a clamp should always be employed to hold them till the pivots are inserted. The guide is a small, flat, steel bar, 3 mm. wide, fixed

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to a handle at an angle in order to keep the hand out of the line of slight; it is introduced for a few millimeters into the meatus and held there. A probe, at a similar angle with its handle, fits into the cone and projects 2 or 3 mm. beyond it, affording a finer point for entering the orifice of the meatus. There is a slot in the disc of the cone which fits the guide and slides readily along it if held in the right position, which is with the point of the probe in contact with the guide. The latter being held in the meatus with one hand, the probe with the cone on it is held in the other and the slot in the disc applied to the heel of the guide and then slipped along it, the point of the probe being kept in contact with the guide; if this is attended to, the cone slides easily into the meatus—if it is not kept to this line, it will jam. When the cone enters the meatus, it is pushed on as far as the disc will permit and the guide withdrawn simultaneously. The probe serves to hold the cone in the meatus till the clamp (Pl. III, 20) is applied, and is then removed. The same manœuver is repeated on the other side, and until the head is introduced into the frame both cones are kept in position by the clamp, which is then removed. It is convenient to have the guide in case it is required, but if the cone is mounted on the probe it can generally be introduced with little difficulty, and the guide is not necessary. There is not room at the apex of the funnel of the pinna for both speculum and cone at once, but the orifice of the meatus can be exposed with the speculum and, while it is withdrawn, if the pinna is drawn well out, the probe carrying the cone can be directed to the opening.

Plate II.—The Mask

The posterior border of the basal horizontal zero plane, represented by the interaural line, having been brought to the level of the upper surface of the horizontal frame or head-vice, the front part, represented by the lower borders of the orbits, is similarly adjusted. This is effected by a face-piece or mask in which two recurved brackets (9) hook over the lower margins of the orbits and are retained in that position by a bit (8) which passes into the mouth behind the upper canine teeth. The bit is a flat brass bar, perforated near both ends with slots which are long enough to allow for differences in the distance between the eyes, and through these slots screws (16) descend from the brackets; split nuts (11) can be rapidly applied to the

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screws below the bit and one or two turns are sufficient to fix the brackets against the counter pressure, acting through the bit, on the teeth of the upper jaw. In fact, the brackets and the bit grip the upper jaw between them like the blades of a pair of forceps. Projecting horizontally outwards from the sides of the mask are two arms (14) which are brought into contact with the lower border of the horizontal frame when this is lowered over the head. When they are in this position, the under surfaces of the brackets and therefore the lower margins of the orbits, which are in contact with them, are level with the upper border of the head-vice and the whole of the basal horizontal plane of the head exactly coincides with the upper surface of the horizontal frame of the instrument. The horizontal arms are secured in position by two clamps (Pl. VI, 46, 46). The distance between the orbital brackets can be adjusted to that between the eyes by a sliding joint and screw (17 and 18).

Plate III.—Cat's Head with Mask, Side View

View, from the side, of a cat's head with the mask and ear plugs in position ready for adjustment in the frame of the stereotaxic instrument. The ear plugs are held in position by a clasp (20) which is removed after the head is adjusted.

Plate IV

A front view of Plate III.

Plate V.—Horizontal Frame or Head-Vice

This is a rectangular brass frame consisting of a frontal, an occipital and two lateral bars, connected by joints and large enough to admit the head of a large cat or rhesus monkey.

The upper surface of the frame represents the basal zero plane of the cranium and is adjusted and fixed so that it exactly coincides with it. The adjustment is provided for: (1) By the aural pivots (25), the inner extremities of which are tapered to fit the ear cones and their centers, corresponding to the interaural line, are level with the upper border of the horizontal frame; (2) by the mask (Pl. II) which brings the lower borders of the orbits to the same level; and (3) the head is centered sagittally and secured by four graduated screw clamps (27, 30). The pivots slide in joints (36) fixed at corresponding points

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on the lateral bars (22) of the frame; the latter are graduated throughout their length in millimeters which are read forwards and backwards from the interaural line; this is their zero point and all movable joints which slide on the lateral bars are secured by screws at corresponding points on both sides. The four clamps (27-30) for fixing the head terminate internally in "grips" (29, 32), small plates provided with three steel points to pierce the skin and hold against the bone without penetrating it, and the two pairs are somewhat differently arranged. In the anterior or temporal pair (29), the plates are triangular, with one point above and two below, engaging the zygoma which lies between them. The posterior or mastoid pair (32) are applied to that prominence immediately behind the meatus. The adjustment of the cranium with these clamps and the selection of the best pattern for the purpose have been a source of some trouble. They were unsatisfactory in the old instrument, where, after trying a variety of grips, I adopted, for each of the four clamps, a single rather obtuse-angled steel point rotating at the end of a screw which perforated a sliding joint on the lateral bar, fixed where it was required. The form of both grip and clamp is defective. A single screw passing through the sliding joint is not rigid enough, it is very slow and under pressure the points do not rotate readily and are apt to twist up the skin and sometimes to deflect the head. The occipital region of the cranium in many animals, and notably in the cat, is in the form of a wedge in two planes; that is to say, in the horizontal plane the apex of the wedge is directed backwards, in the frontal plane downwards. With single blunt points and the force applied entirely by screws, there is a tendency to lift the head with the bilateral pressure, and if sharper points are used to obviate this, they may penetrate the bone to a variable depth. These defects have been removed. The plate, carrying three points which form the mastoid grip, is inclined in two planes like the mastoid itself, so that all three points engage it.

Adjustment.—Instead of being carried by a single screw, there are two bars which perforate each sliding joint (35, 37); one above and one below the horizontal frame. Internally, *i. e.*, medially, the two bars are attached to the grip (29, 32); externally, their extremities are united by a short plate. The center of this cross-plate is perforated and gives passage to a triple-thread screw which is fixed by its inner extremity to the sliding joint on the lateral bar. This screw, therefore, is parallel to the sliding bars which carry the grip and lies

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between them. A nut (28, 31) is fitted to the outer end of the screw and works up to the cross-plate. The sliding bars, with the grip at one end and the cross-plate at the other, form a rectangular frame which slides to and from the median plane, towards which it is driven by the screw-nut. It is pushed in till the grip is in contact with the skull, the nut is run up rapidly on the screw till it reaches the cross-plate and then effects the final adjustment and fixture of the head. All the four clamps are made in this way, millimeter scales are engraved on the surfaces of the upper sliding bars, as well as on the aural pivots, and are arranged so that all six scales can be easily read from the same point in front and rapidly compared, which ensures accuracy and saves time.

The clamp (20) for holding the ear cones in position assists in adjusting the head on the aural pivots. When the frame is lowered over the head, the latter is raised till the ear cones are opposite the pivots, which are then pushed home, the horizontal arms of the mask being brought almost into position below the horizontal frame by the adjustment of the pivots and cones; all that remains is to hold the arms in contact with the lower border of the frame, slip the clamps (46) over them, noting that they are equidistant from the pivots on both sides and fix them. The occipital bar (24) is brought into contact with the occiput and its sliding joints (38) and those of the four clamps (35, 37), are fixed by the screws at corresponding points on the lateral bars (22). The opposed clamps are then adjusted in pairs, the grips are pushed up, the nuts run up the triple-thread screws and one or two turns will suffice to hold the head firmly, with identical readings of the scales on both sides; the aural pivots are made to correspond and carefully inspected to see that they and the cones are well home. From the accessibility of the head in the frame its position can be thoroughly inspected after it is fixed and any error ought to be detected and corrected before the cage and travelling stage are applied.

Plates V, VI represent the basal horizontal frame or head-vice as seen from above.

V. The frame from above.

VI. The frame with the mask and ear plugs in the position they occupy in the frame, but without the head.

VII. The same as VI, but with a cat's head in position.

VIII. The same head in position viewed from the side.

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Procedure.—The next steps in the procedure are the application of the cage, measurement of the head, comparing its dimensions with those of the standard, setting the extensible scales accordingly and fitting them in their places. The traversing stage, with the pilot needle, is applied to one of the surfaces of the cage and fixed with clamps. The pilot needle is brought into the correct position in contact with the cranium, which is marked with the drill, then trephined and the pilot racked down to the selected point. The electrolytic or other form of operating needle is then substituted and the operation completed. It will be convenient to describe the extensible scales next, as they appear in the illustrations of the cage, and their application follows immediately in the order of operative procedure.

Plate IX.—Extensible Scales

Each scale consists of a fine spring enclosed in a tube open down one side to expose the spirals which can be made to measure millimeters, or more, or less. The spring is fixed to the tube at one end and at the other to a screw rod (57) which passes through the neck (58) into which the tube is drawn and through three milled heads (Pl. IX 59, 60, 61). The proximal one (59) moves the spring as a whole so that, after it has been set, any particular spiral can be brought opposite the zero of the millimeter scale without moving the tube or altering the extension of the spring. The middle milled head (60), which fits over the elongated neck (58) of the tube, tightens or relaxes the grip of the latter on the screw rod which passes through it. The rod can be drawn in and out and the spring extended or contracted and fixed anywhere by screwing the head up. It is convenient, while the spring is being set, to fix this head sufficiently to make the spring retain any position given to it, but not to prevent its adjustment. The third (distal) milled head (61) fits the screw rod and serves as a fine adjustment for the spring, but of course can act only when the middle head is relaxed. To facilitate reading, the spirals are painted black and white in alternate groups of five and an ivory millimeter scale, also marked in groups of five, is attached to each scale by spring clips. These ivory scales are not absolutely necessary, but are added to facilitate reading and the division into groups of five is a great assistance for this purpose; they are adjusted to correspond with the permanent scales on the instrument and the

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extensible scale is between them. The zeros of all these scales are made to coincide and the index reads their divisions simultaneously.

All measurements are from zero and the operator requires to know how far the point of the needle is from each of the three zero planes. On this triple scale he sees at once how far the needle is from the zero plane from which it is counted in millimeters, by the engraved scale on the instrument and the ivory scale which is identical with it, and at the same time how far in coordinates, or corrected divisions, shown by the spirals of the spring.

In practice, the extensible scale is set, so that the divisions of the spiral spring bear the same relation to millimeters as the dimensions of the cranium of the experimental animal do to the standard. The number of divisions is always the same as the number of millimeters in that dimension of the standard, but they may measure millimeters, or more, or less, just as the whole dimension may be the same, or more, or less.

Gauge for Setting Scales.—For setting the scale, it is convenient to have a gauge with a millimeter scale and two clamps which hold the tube parallel to it. Between the scales are two sliding double indices which point both ways, one point reading the millimeter scale, the other, the spirals of the extensible scale; their use will be best explained by an example. The transverse dimension from the zero plane to the surface of the standard head in the cat is 21 mm.; hence, this diameter must always be divided into 21 units, whether millimeters, or more, or less. Suppose the same diameter of the experimental cranium is 19 mm. the indices are set 19 mm. apart on the millimeter scale; the spiral spring is then adjusted till 21 spirals are included by the opposite points of the same indices; *i. e.*, the 21 spirals measure 19 mm. If, on the other hand, the diameter had been 24 mm. the 21 spirals would have been made to measure 24 mm.*

There are one or two practical points to be observed in setting these scales. A spring fixed at one end expands rather more, when it is extended, at the free end than at the other, and if it is simply extended to the required length, there may be an appreciable difference in the divisions at the two ends. This can be corrected by extending the spring till the intervals near the fixed end are slightly greater than their final measurement and then letting the whole spring gradually

* An illustration of this gauge has been published in the Atlas, Part I.

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contract till they are correct. The edge of the slit in the tube is graduated in 5 mm. divisions and, if the spring is set to measure millimeters, it can be seen whether the spirals are uniform and, with a little practice, they can be set correctly without difficulty. The scale should always be set, in this way, to measure millimeters before it is finally adjusted to a proportional scale; the alteration required is usually slight and the possible error minute, but even then it is better to overextend the spring slightly and let it drop back. After all, it is not the defect of a fraction of a millimeter that matters, but the cumulative error which occurs without an extensible scale and may sum up to several millimeters.

When fixed in the instrument the spiral selected for zero must be made to coincide with the zeros of the millimeter scales and the index reads them simultaneously. This adjustment is effected by the first milled head, as previously explained. As the travelling stage is applied to the top of the cage in four different positions, the operator must make sure that the scales are applied to the diameters of the head for which they were set.

Plates X, XI and XII.—Cage and Traversing Stage

The above plates give a general view of the instrument with the needle applied in three different positions.

X. Shows the cage with the traversing stage (69) applied above it, secured by clamps (90) and the needle in its holder in the vertical position. This is the first position, the needle-holder facing forwards. In the second position, the traversing stage is exactly reversed and the needle faces backwards. All the three extensible scales with the ivory ones attached are in position. There are two movements of the traversing stage and a third of the needle-bed in its sheaths. The quadrant (77) enables the needle-holder to be set at various angles, the inclination in the first position being downwards and to the left (of the head), *vide* Plate XIX.

XI. Shows the traversing stage and needle applied to the left side of the cage, sixth position. It is shown inclined downwards and inwards; *i. e.*, towards the middle line.

XII. Here the traversing stage and needle are applied to the back of the cage, seventh position, the needle is horizontal, but can be inclined downwards and forwards.

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The cage is sufficiently illustrated in the above plates; it requires very little description itself, as it is merely a skeleton table to support the traversing stage which can be fixed to four of its surfaces. It is fastened to the frame by four feet (67, 68); these carry round bolts which drop into the slots (42, 43) in the frame and the feet are locked by screws (44, 45) half cut away to avoid the necessity of removing them and the risk of their being mislaid. So far, the object of the cage is very simple, but its dimensions are important, as they are necessary factors in the measurement of the head and the excursion of the needle. In planning the dimensions of the first instrument of this pattern, realizing the great importance of rigid support, for accurate movement of the needle, and wishing at the same time to keep the machine light, it was desirable, in all positions, to fix the needle as near the head as possible, and the three diameters of the cage were made approximately proportional to those of the cranium. Consequently, the distance from the surface of the cage to the zero plane parallel to it was different, in the vertical, transverse and longitudinal diameters. This involved an element of complication in measurement, for scales and instruments had to be adjusted separately for each dimension. As the whole instrument is now always suspended on springs and supports the head, a slight increase of weight is immaterial. The dimensions of the present cage, from the surface to the parallel zero plane, are identical in all three diameters and no adjustment of scales or instruments for measurement from different positions is required. This simplifies the procedure and the cage has been strengthened sufficiently to allow of the alteration without risk of impaired accuracy.

As soon as the cage is secured, the measurements of the cranium are taken in its vertical, transverse and longitudinal diameters, with the needle gauge (Pl. XXII), described in Chapter V. The measurement of the anterior longitudinal diameter in the cat is discussed in the same chapter.

The measurements of the cranium are compared with those of the standard, the extensible scales (Pl. IX) set accordingly and inserted in the clamps (84, 86) provided for them in the traversing stage (69) and inner sheath (93) of the needle-holder and their zero points made to coincide with those of the millimeter scales.

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Plate XIII

The **traversing stage** is a square frame for carrying the needle and its holder with a graduated movement in three planes, two in the plane of the stage and one perpendicular to it. With clamps and steady pins, the frame can be applied to the free surfaces of the cage in seven positions, four above, that is, facing four different ways, forwards, backwards and to either side, and it can also be fixed to both sides and the back of the cage. It is always fitted so that crossed lines, passing through the zero points of its longitudinal and transverse scales, coincide with the crossed zero lines of a lamella, parallel to it, of the cranium or charts. As it is applied in several positions, the relations of its parts and their movements are subject to similar variations; but for purposes of description, and always unless otherwise stated, it is assumed to be in the first position on the top of the cage (Pl. X), the needle facing forwards, its carrier moving on transverse guides (70*a*, 70*b*), these in turn travelling on longitudinal guides (91) and the terms right and left corresponding to the sides of the head in the machine. So, the movements, like those of the stage of a microscope and effected by rack and pinion, are longitudinal and transverse in the first position, but are reversed when the needle faces left or right; and when the stage is applied to the right, left, or rear faces of the cage, the transverse movement becomes vertical and, in the latter case, the longitudinal becomes transverse. The needle is fixed on a bed (94) perpendicular to the stage, this is moved by rack and pinion in an inner sheath (93), which slides in an outer sheath (72), the latter being pivoted to the needle carrier (71), and with a quadrant scale (77) it can be inclined, at any angle up to 25°, in one direction and in one plane; but since it can be brought to any plane by the movements and positions of the stage, a large choice of positions, inclination and movements is provided.

The changes of direction on the top of the cage are introduced only for the purpose of varying the angle of inclination; for a vertical needle, one position is sufficient. In the first four positions referred to it can be inclined downwards and to the left, downwards and to the right, downwards and forwards and downwards and backwards, respectively.

In every position the crossed lines, real or assumed, are the identical zeros in stage, chart and the lamella of the head itself, and measure-

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ments are reckoned from both sides of them in millimeters or coordinates. In the stage, millimeter scales graduated from these zero points are engraved on the transverse (70*a*, *b*) and longitudinal (91) guides; attached to them are extensible spring scales (82, 83) which are adjusted proportionally to the dimension they represent, after gauging the selected head; the spirals representing coordinates, which bear the same ratio to millimeters as the whole dimension does to the standard. Ivory millimeter scales (88, 89) are also attached to the guides. Thus, there are three sets of scales for each movement, the engraved scale on the guide, an ivory one and the extensible scale between them. They must always be adjusted so that their zero points coincide and the same index reads them all simultaneously, keeping the observer informed of the number of millimeters and coordinates between the needle and the zero plane to which the scales relate. Ivory scales are not absolutely necessary and can be dispensed with; they were introduced because brass is so easily tarnished and stained in operations that it is sometimes difficult to read the scales on the guides. In future I propose to employ white metal not so easily affected which will I think make the ivory scale superfluous.

Direction of Needle.—The carrier (71), with the needle in it, is racked with transverse and longitudinal movements from either side of the crossed zero lines of the stage and any parallel lamella of the cranium and it is easy to bring the needle opposite to any selected point in the latter by these movements. The selected point must lie in at least one lamella in each plane; if we locate it in one parallel with the stage, we can imagine the chart of this lamella used like a lantern slide and inserted in the place of the actual lamella in the cranium, its ruled zero lines coinciding with crossed lines drawn between the zero points of the stage. We identify the objective point by measurement from the two zero lines of the chart lamella and move the carrier the same distance from the corresponding zeros of the stage. The needle must then be opposite the objective and it only remains to rack or slide it up to that point. The measurement of the projection of the needle will be described in another section. In the example given, where the objective is located in a lamella perpendicular to the needle, the function of the stage is to bring the needle opposite the objective point by two movements, leaving the third, the projection of the needle, to bring it to the required point; but the objective may be located, if preferred, in a lamella perpendicular to the stage

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and parallel to the needle. In that case one movement of the stage brings the needle to the edge of the lamella, the second brings it into line with the objective, which is reached by the projection of the needle; as, for example, one movement might bring a needle in the same plane to the edge of a certain page in a book, a second movement to a particular line on that page, and the projection direct it to a particular letter. This method is adopted with the inclined needle, and will receive more detailed explanation elsewhere (Chapter V); but it may be mentioned here that, as the needle can be inclined only in one plane, the objective point must be located in a plane parallel to that inclination and therefore perpendicular to the stage. The needle is brought to the edge of the selected lamella by one movement of the stage, as if the lamella were the page of the suggested book; by the second movement of the stage and the projection of the needle, it would be easy to bring the point of the latter to any letter on the page if they were visible. Thus, of course, they are not in the cranium, but it is practicable in the indicator described in Chapter VI, where all the parts are represented and in view, and the movement can be copied and repeated in the operating machine. It should be noted that one movement of the stage measured by its corrected scale brings the needle to the edge of the lamella; the other two movements are determined in the indicator, and are merely copied in the machine by corresponding scales in which millimeters, not coordinates, are employed, any corrections required having already been made in the indicator.

A mechanical detail connected with the stage must be mentioned. Both transverse guides (70*a*, *b*) have millimeter scales engraved on them. In one, the posterior (70*b*), the zero is at the center, *i. e.*, halfway up the guide, and the scale is graduated from it on both sides. On the anterior guide (70*a*) the zero is at the end, the scale is graduated towards the center and the syllable *Trans.* is also engraved, indicating that this scale is used when the needle is directed transversely, as it is when the stage is applied to either side of the cage (positions 5 and 6). The scale on the posterior guide, which is employed in all other positions, is not available when the stage is applied to either side (5 and 6). In the first four positions, where the stage is above the cage, the zero of the posterior guide, which is in the middle, coincides with either the frontal or sagittal zero plane of the instrument and head. When the stage is applied to the rear face of the cage and

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the transverse guides are vertical, again this median zero is level with the upper border of the horizontal frame and the basal zero plane. But the stage cannot be applied to the sides of the cage at this level (positions 5 and 6), owing to the clamps and screws of the lateral bars, and it must be applied with the edge of the stage resting on the horizontal frame (see Pl. XI). This is the vertical zero, and obviously cannot be measured by the scale of the posterior guide, as its zero point cannot be brought down to this level; hence, the scale of the anterior guide is used for these two positions 5 and 6, and is read upwards from a zero level with the upper surface of the horizontal frame or head-vice.

Seven Positions.—The beginner may experience some little difficulty in recognizing the seven positions in which the stage is applied. The illustrations will assist him and, in addition, the following points. The four positions on the top of the cage are identified by the aspect of the needle which may face forwards, backwards, or to right or left. In the three remaining positions the transverse guides are vertical and the needle horizontal. Held in that position, the projecting quadrant scale (77) may be above the needle, or below it; it should be above in all the positions, so that the point of the needle can be inclined downwards. If the stage is held with the transverse guides vertical and the quadrant above the needle, it can be applied in that position to the right, left, or rear face of the cage, resting with its edge on the horizontal frame in the lateral positions 5 and 6; but in the seventh position, behind, the central zero of the posterior guide must be level with the upper surface of the frame. When applied as directed, the steady pins will fit into the holes belonging to them, and the stage must be secured with its two clamps.

Plate XIV.—The Needle-Holder

In describing the **needle-holder** it is assumed to be in the first position (Pl. X), standing vertically on its point, the face of the ivory bed (94) looking forwards, the locking screw (96) at the top and the extensible scale (111) on its right.

Its object is to carry various needles, with their special adjustments and, in the case of the electrolytic needles, with electrical connections, in a plane perpendicular to that of the travelling stage and to one of the three zero planes of the instrument and the cranium. On the

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right side, the scale (112) for recording rectilinear movements is attached and set, so that the distance of the point of the needle from the zero plane to which it is perpendicular is always shown, and when the index reaches zero the point of the needle is at the zero plane. On the left, the indicator scale (110) for inclined movements records the length of needle projected from pivot to point.

The needle-holder consists essentially of a bed (94) and two sheaths, an inner (Pl. XIV, 93) and an outer (Pl XIII, 72). The bed, which is made of ivory for the electrolytic needle and of brass for the others, has the needle and its special appliances attached to it and travels in the inner sheath by a rack and pinion movement, which may be regarded as a fine adjustment; on the right (rectilinear), its excursion is registered by an adjustable index (113) attached to the bed and by extensible (111) and ivory millimeter scales (112), fixed close together on the inner sheath. The index reads both at once and they have the same zero, which always corresponds to the zero plane to which the needle is perpendicular, *i. e.*, when the point of the needle is at that zero plane, the index is at zero on the scales, so that the index always records the distance of the point of the needle from the plane in millimeters and in divisions of the spiral scale at the same time. These are called scales of the rectilinear needle. The inner sheath slides in the outer, which is pivoted to the carrier of the travelling stage (Pl. XIII, 71). It is provided with a graduated quadrant and clamp by which the needle can be directed and fixed at various angles. With inclined movements we employ the indicator scale on the left, which records the length of needle projected in millimeters only. The sliding movement between the inner and outer sheaths serves as a coarse adjustment for the excursion of the needle and can be arrested and locked at any point by the milled head (96) above the holder.

The inner sheath, which is made of brass, terminates at its lower extremity in two jaws together forming a blunt point called the stop (97). The jaws, which spring apart sufficiently to admit the needle, are brought together by a tension screw (99); they are lined with ivory, and grooved in the center for the needle, which is thus supported close to the cranium. The sliding movement of the inner sheath, which includes the stop, also carries the bed and the needle with it, while the rack and pinion project the needle through the stop.

These arrangements and movements, the sliding between the sheaths, the racked projection of the bed, the quadrant regulating the inclina-

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tion of the outer sheath and therefore of the needle and the scales by which the movements are regulated, which will be described immediately, are applicable to all varieties of needles, but two or three different forms of bed are adapted to the particular objects of the needles attached to them. The beds all fit the inner sheath and can be easily interchanged, a necessary provision, as no matter what needle is employed it is always preceded by the pilot needle (Pl. XVI, 1), a plain steel needle tapering to about the same caliber as the one which follows; it penetrates membranes, is not easily deflected and traverses structures with little injury. As soon as it has reached the required point, it is retracted, the bed to which it is fixed removed and an operating needle, already mounted on its bed, substituted. The pilot needle requires no manipulation beyond its linear projection and is always kept mounted on a plain brass bed engraved with scales, but with no other fittings. With all forms of steel cutting needles, cyclotomes, spherotomes, etc., requiring some manipulation for projection and withdrawal of the concealed knife, rotation, etc., a special bed (Pl. XVI, II) is necessary; it is suitable for any of these needles and they can be quickly attached and removed.

The platino-iridium needles sheathed in glass which are used for electrolysis and stimulation are mounted on an ivory bed with electrical connections.

A general account of various needles was given in Chapter I, p. 17, as their application and use form the essential object of the stereotaxic method and instruments, but it is advisable to add a detailed description of the needles and the beds on which they are mounted in this chapter.

Beds for Pilot, Cutting and Insulated Needles.—Three different forms of bed are used and represented in the plates. They all fit the inner sheath (93) of the holder, and when racked down by the milled head (95) the needle which is attached to them is projected through the stop. Those for the pilot and cutting needles are made of brass, but the bed for the insulated needles used for electrolysis or stimulation is made of ivory and fitted with adjustment for the glass sheath and wires and electrical connections.

Bed for Insulated Needles.—This bed is shown in the illustration fitted in the inner sheath (93) of the holder, forming part of an arrangement for fixing special needles and also for directing and measuring their movements and fulfilling their special requirements.

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The coarse or fine projection movements of the needle have been referred to and their measurement will be fully described (Chapter V). They are required for all forms of needle and are secured by the sliding and racked movements of the inner and outer sheaths and the bed and the inclination of the carrier which are available with all varieties of bed, and these parts are indicated in the illustrations by the same numbers. But the special requirements of different forms of needle cannot be provided by a single bed and the varieties alluded to will now be described. Special means are required for fixing the glass and platino-iridium needles, for the connections of the wires for the passage and insulation of electrical currents for electrolysis and stimulation and the rapid adjustment of the wires for these purposes. The provisions which this bed has to meet may be enumerated as follows:

1. For fitting the glass needle quickly and accurately and replacing it if it should break.
2. For connecting the wires of the needle with the leads from the battery or switch.
3. For bringing the stop into circuit when required, "live stop."
4. For adjusting the length of the wires and their projection from the point of the glass needle.
5. Against short-circuiting by water.

These requirements are met by the following arrangements:

The bed (94) is made of ivory and has an adjustable index (113) for reading the rectilinear scale on the right, and on the left is the scale for the inclined needle (110).

Clamps.—It is important that all clamps which hold the needle should open from the front (or from above, if the holder is lying on its back) so that the needle can be laid on its bed at full length. It is inconvenient to pass rigid and fragile glass needles through holes or under clamps. It is so much easier to make clamps with screws which pin the needle to the bed that it has been difficult to abolish them, but in the present holder lateral clamps are employed. The jaws of the stop (97) are first separated; next a pair of jaws (102, 102) are opened by two eccentric cams (103, 103). Each of the milled heads of the cams has a line marked on its anterior surface, and when the two lines are at corresponding angles, the jaws are equidistant from the middle line; in other words, they center the needle. A small piece of fine rubber is drawn over the needle between

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these jaws and secures a firm hold without the risk of fracture. At 104-105 there is an arrangement to prevent short-circuiting. The wires leave the double glass tubes almost touching one another and may be short-circuited by a drop of water. It is not necessary to sluice the needle with hot water and the free douche is bad for animals and instruments, but if it is resorted to, a provision of this kind is indispensable. The accident is prevented by the ivory wedge (105) tapering to a knife-edge which passes between the wires till it is in contact with the glass. Before the needle is placed in position, the arm (104), which is fixed on a pivot, is swung out of the way. A small piece of thin rubber, with a notch in it to receive the edge of the ivory wedge, is first laid on the ivory bed, the needle on this, and a second piece of rubber, like the first, is laid over the needle. Then the arm (104) is swung back to its place; it carries, on a screw, a small plate with a notch like the pieces of rubber and which also like them receives the edge of the ivory wedge; then the whole is secured by two or three turns of the screw. The end of the glass needle and its two wires are sandwiched between the bed and plate and the two pieces of rubber; the latter project a little way on both sides of the wedge and being in firm contact no water can pass between them.

The wires, which can be seen on both sides of the wedge, drop into slits and are gripped by clamping screws in brass sliding shoes (107, 107); the *terminals* (108, 108) which receive the leads from the switch are fixed to the same shoes, establishing a connection between the leads (116, 117) and the wires of the needle. The shoes are attached to screws (109, 109) and by means of two small drums with milled heads, which can be worked easily with the tip of one finger, the shoes, and therefore the needle wires, can be projected and withdrawn and the wires at the needle-point adjusted with great nicety.

The millimeter scale (110) on the left of the bed, which is used when the needle is inclined, is read by an adjustable index seen in Plate X, 79. This and the extensible (111) and ivory millimeter (112) scales of the rectilinear needle, which have been mentioned, will be more fully explained immediately. Three leads are seen (116, 117, 118). At one end they are connected with the switch (Pl. XII, 140); at the other, two of them with the shoes and so with the wires of the needle, and the third with a terminal (101) which can be connected by a shunt (100) with the metal jaws of the stop. The shunt is not absolutely necessary, since the leads can be disconnected

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at the switch, but it is an additional precaution. It is useful to be able to bring the stop into circuit when faradic currents are applied for the stimulation of deep centers or tracts. When these are excited with an insulated needle, it is often difficult to decide whether the response is genuine, *i. e.*, originates at the point directly stimulated and can be regarded as evidence, so far, of a function of that structure, or whether it is really elicited from some more excitable area near enough to be affected by what is called escape. It is not always possible to settle that question. In some cases, by numerous experiments in different animals with currents of various strength and by comparing the results with those obtained by direct stimulation of the suspected areas, a fairly definite conclusion can be reached. Considerable assistance may be afforded by having at hand a means of quickly changing the circuit so that different structures are implicated. As a rule, the shorter the arc the better; there is less chance of other structures being involved, so it is generally advisable to use the double-barrelled or the concentric needle with an arc of little more than 1 mm. between the points. If the stop is employed, it must be in contact with the surface of the brain, then, by a single movement of the switch, one of the needles can be disconnected and the live stop brought into circuit by the lead at 118. The current then passes through the brain between the stop and the point of the focal needle. Another movement of the switch disconnects the live stop, brings the whole instrument into circuit and the current passes between the focal needle and all the points of contact of the instrument with the surface of the cranium. Without any loss of time, therefore, these three variations of the circuit can be tried immediately one after the other, the results compared and useful information may be obtained. It is obvious that, if there is escape, it is more likely to occur under the latter conditions, with an extended and diffused arc; hence, if the response is more marked under these conditions the probability of the first result having been due to escape is increased. There may also be some difference in the character of the response and it is an advantage to have these alternatives provided for.

Pivot Stop Line.—On the back of the inner sheath of the holder there is a transverse line on which the letters *P. S.* are engraved; they stand for the words "pivot stop" and indicate that when this transverse line coincides with the top of the external sheath, the point of the stop is level with the center of the pivot. The needle is inclined

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by rotation on this pivot, which is the zero from which its length is measured; this must be known to make the operating needle correspond with the finder of the indicator.

Plate XV.—Insulated Platino-Iridium Needle

Platino-iridium needles insulated in glass tubes are employed for electrolysis and stimulation; one of the double-barrelled variety is shown, mounted, in the illustration of the needle-holder.

I have not made any alteration in the three varieties of these needles which I designed, and of which a description has been published (1). They comprise the single needle (1), the double-barrelled needle (2) and the concentric needle (3).

For electrolysis the single needle is nearly always used. It is easily introduced and makes a smaller wound than the others. Any size may be selected and the exact amount of wire protruding precisely regulated by the attachment of the sliding shoe (107). With these variations and regulation of the intensity and duration of current, the exact size of the lesion required can be accurately controlled with a little practice. The anode should always be employed if precise circumscribed lesions are desired. With a wire of 0.3 mm. diameter, projecting 1.5 mm., and 5 ma. current, for 20 seconds, a spherical lesion of about 2 mm. in diameter can be obtained.

The head-vice, with its numerous points of contact, serves for the indifferent electrode, or a pad saturated with saline solution may be applied to any part of the skin.

If it is desired to make an electrolytic lesion in a structure from which some response to excitation can generally be elicited, it is usual, after introducing the needle, preferably the single one, to try the effect of a preliminary stimulation to verify the position. In this case, and, as a rule, when the single needle is employed for stimulation, it should be used with the live stop, which must be in contact with the surface of the brain; but must of course be disconnected for the electrolysis, or it would produce a cathodal lesion of the cortex.

But for excitation generally, the *short arc* affords the best chance of avoiding escape and one of the double needles should be employed, corrected by varying the circuit in the way already described.

The glass sheath of the double needle is made by fusing two small tubes together for a short distance and then heating and drawing them

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out. For the double-barrelled needle (2) they are brought to a point on a fine carborundum wheel and the ends of the wires ground parallel with the orifice. In the concentric needle (3) one wire is pointed and projects from the end of one of the tubes, as in the single needle; the other glass tube is ground away two or three millimeters below its fellow and the wire from the second tube is flattened and fused into a little collar, about 1 mm. broad, which encircles the first tube about 1 mm. from its extremity, the point of the first wire being separated from the collar by about 1 mm. of glass tube, the current passing between the point and the collar. In all the needles, by the attachment of the wires to the shoes on the needle-holder, the exact adjustment of the termination of the wires, their relation to one another and to the ends of the glass tube can be easily regulated. The double-barrelled needle traverses tissues more readily and makes a smaller track than the concentric, but the latter gives a more equably diffused current, which is advantageous for the stimulation of groups of cells. When the operator desires to mark the point at which a particular response was elicited, either of the needles can be employed for the purpose. The apparatus should be kept arranged so that a galvanic current from a battery with a milliamperemeter and rheostat, and also a faradic current from an induction coil, can be switched on or off and interchanged at pleasure; by the switch on the instrument it can be directed into one or both of the wires of the needle and the size of the lesion determined. If both wires of the concentric needle are brought into circuit, a lesion of considerable size is quickly formed.

The following table gives some idea of the sizes of the needles and glass tubes commonly used:

	Standard wire gauge (British)	Diameter in mm.
1. Single needle, fine	32	0.19
Glass tube for same	27	0.34
2. Single needle, large	25	0.45
Glass tube for same	21	0.70
3. Double-barrelled needle	30	0.27
	30	0.27
Glass tubes for same	24	0.50
	24	0.50

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PLATE XVI.—OPERATING STEEL NEEDLES AND BEDS

This plate shows some steel operating needles and the beds for them.

I. The pilot needle with its bed in which it is kept mounted as it is always required.

II. The horizontal cyclotome mounted on a bed which serves for the other forms of cutting needle shown at III and IV, and a fine tube (V) provided with a funnel and a rod which fits it and is used for introducing drugs.

III. Orthotome.

IV. Dr. Mussen's spherotome.

V. Fine steel tube for introducing drugs.

PLATE XVI, A

A drawing of an improved form of bed for these cutting needles which has not been constructed yet.

PLATE XVII

Separate drawings of some of the cutting needles at present constructed.

The instruments enumerated above must now be described more fully.

PLATE XVI.—OPERATING NEEDLES AND BEDS

1. The Pilot Needle.—It is advisable that the introduction of all insulated or cutting needles should be preceded by a plain steel needle of slightly greater caliber than that which follows; it makes a smoother track, is less easily deflected than glass needles, and if membranous structures are encountered, this is important; the dura can be perforated without an incision and, on the whole, it contributes to smaller lesions and greater accuracy. Two or three sizes should be available and a suitable one fixed in the clamp on the special bed shown in the illustration. After the pilot has been introduced, it is withdrawn, the bed removed from the inner sheath and a special needle already mounted on its bed substituted.

2. Cutting Needles.—These are hollow steel needles such as are used for hypodermic injections, but with blunt points. A wire or fine watch-spring knife can be projected a few millimeters from a slot near the point, and then by rotating the needle, or projecting or retracting it a short distance, various small localized lesions or

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incisions can be produced. The smallest needles of this kind which I have used are 1 mm. in diameter and the knife can be projected 4 mm., cutting a disc when rotated of 9 mm. in diameter and of any size below this. But for some purposes the finest hypodermic needles from which a steel wire can be projected 2 or 3 mm. may be employed, and very precise and restricted lesions can be produced in deep structures like the central ganglia with such trifling injury that it can be ignored and the conditions apart from the lesion regarded as normal.

The following varieties of these needles are available at present:

1. The Horizontal Cyclotome.—(Pl. XVI, II.) A fine watch-spring is projected almost horizontally from a slot in the side of a needle, 1 mm. in diameter, close to its extremity. The knife can be projected any distance up to 4 mm. and when rotated cuts a disc perpendicular to the needle of any diameter up to 9 mm.

2. The Vertical Cyclotome.—(Pl. XVII.) This can be made of various sizes in accordance with the object for which it is required. A hollow needle, 1 mm. in diameter, is divided by a longitudinal incision for from 2 to 5 mm. from its extremity, a flat watch-spring knife, slightly shorter than the incision which it occupies, is pivoted about its center by a small rivet; the wire which passes down the needle is pivoted to the proximal end of the knife. When introduced, the knife is entirely concealed in the incision, in which it lies parallel with the needle; by pressure on the wire, the knife is made to rotate upon its pivot until it projects at right-angles to the needle, an equal distance on both sides of it. In reaching this position it cuts two diagonal quadrants and by retraction of the wire the knife regains its original position; the needle is then rotated half a turn and the knife again projected till it is horizontal; it thus cuts two other diagonal quadrants complementary to the first and completes a disc the plane of which is parallel to the axis of the needle, the diameter being the same as the length of the knife.

3. The Orthotome.—(Pl. XVII, 137) is like the last, but instead of the knife being pivoted on its center, the rivet is at the distal end, and when pressure is applied to the wire the knife projects horizontally from one side of the needle and in its movement to this position cuts a quadrant; if the needle is projected or withdrawn a few millimeters the knife makes a linear incision of its own length parallel with the needle.

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4. The Spherotome.—(Pl. XVII, 138) designed by Dr. Aubrey Mussen. Here a steel wire ending in a watch-spring knife is introduced into a hollow needle. The extremity of the knife rests in a slot close to the end of the needle and is there pivoted with a rivet; one side of the needle for a few millimeters from its end is filed away to expose the watch-spring which bulges outwards in the form of a bow when pressure is applied to the wire. By rotating the needle when the spring projects, a spheroidal figure is cut, the size and shape of which depend on the length of watch-spring exposed and the pressure applied to it.

5. Fine Steel Tube for Introducing Drugs, etc.

I. Pilot Needle Bed.—This needle has no movement but linear projection and retraction; it is therefore clamped (120) to a brass plate with a rack along the right edge which fits the inner sheath (93) of the holder (Pl. XVI) and can be projected by the racked and sliding movements described. It is provided with an adjustable index (113) on the right for reading the rectilinear scales and a millimeter scale (110) on the left for inclined movements. A screw head (118) serves as a handle for introducing it or removing it from the inner sheath.

II. Bed for Cutting Needles.—For all these needles the same linear projection movement to direct them to any required point in the brain is necessary and is provided for by the same means; *viz.*, a brass plate fitting the inner sheath and with an adjustable index and scales similar to those which have just been described with the pilot needle. But when these needles have reached their destination some mechanism is necessary for their special purpose, such as projecting a concealed knife a short measured distance, rotating the needle and knife a half or a full turn and then retracting the knife before withdrawing the needle. The bed which is at present employed for this purpose is shown in Plate XVI, II. A design for an improved pattern is shown in Plate XVIA, but owing to the war it has not been possible to get it made. It will be necessary to describe both patterns, beginning with the one in use.

Plate XVI, II. The inner sheath and scales are the same as those in Plate XIV and these parts are indicated by the same figures. The brass bed similar to that of the pilot needle will also be recognized and the projection of the concealed knife and the rotation of the needle are effected by the following arrangement. The operating needles

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shown in Plates XVI and XVII have the same construction and consist of:

(1) A hollow steel needle about 1 mm. in diameter with an opening close to the distal end through which the concealed knife (7) is projected and terminating at the proximal end in a brass cylinder (2), about 2 mm. in diameter and 10 mm. long, terminating at both ends in milled discs (3 and 9). These parts are united and rotation of the discs rotates the cylinder and needle also. The cylinder is prolonged above the disc (3) and graduated in mm. (4). A second rather larger cylinder (5) screws over (4) and its lower margin serves as an index to read the graduations on (4). The cylinder (5) is screwed down by the milled disc (6) and carries a wire which passes down the hollow needle and is attached to the knife (7). Consequently, when the cylinder (5) is screwed down, it projects the knife and at the same time its lower edge shows on the graduations at (4) the distance the knife is projected. The cylinder (2) is held by a clamp (119) fixed to the bed, the pressure of the clamp is regulated by a screw; the friction should be sufficient to hold the cylinder firmly, but not to prevent its rotation. The two milled discs (3 and 9) prevent any slipping in the axis of the needle which passes through the stop (97).

The projection of the needle is measured and the adjustable indices set by the stop in the same way as with the glass needle explained under Plate XIV, and a mark on the disc (3) shows the direction in which the knife is projected; *i. e.*, it corresponds to the opening in the needle. Before the needle is introduced, the knife is withdrawn so that its extremity is flush with the opening in the needle and the scale at (4) is noted. When the needle has reached the required point in the brain the disc (3) is rotated till the mark on it faces the direction in which the knife should be projected; then the disc (3) is steadied with a finger of the left hand and the disc (6) rotated with a finger of the right, causing the cylinder (5) to travel down on (4), the scale showing the excursion of the cylinder (5) and the distance the knife is projected. If it is necessary to rotate the knife and needle, this is effected by rotating the disc (3), the mark on which shows the amount of rotation, usually a half or a full turn being required. The operation having been completed, the knife is retracted by repeating the above procedure in the reverse direction and the needle can then be racked out and removed. There is no great difficulty about this

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procedure, but the method of holding one disc and rotating the other, the regulation of the friction of the cylinder and the recognition of the position of the knife under all circumstances are points which admit of improvement and in these respects the plan adopted in the design XVIA is more convenient, the application of various needles of different sizes is simplified, the movements are more precise and effected more easily and the position of the concealed knife can always be recognized immediately.

Plate XVIA

Design for Improved Bed for Cutting Needles.—It consists of the brass plate (1) fitting the inner sheath and furnished with an adjustable index (2) and scale (3) already described and two structures which may be called cradles, inner (6) and outer (5); they are elongated narrow brass plates with the ends turned up at right-angles to form three sides, the bottom and two ends, of a narrow oblong box; the outer (5), considerably larger, is fixed to the bed (1); the inner (6), supported by pivots (11, 29) in slots (13, 31) of the end plates (7, 8) of the outer cradle (5) in which it rotates. The lower of these pivots is formed by the shaft of the needle (29), held in the slot by a notched and hinged bar (32); the upper pivot is a square rod, the central rod (11), with a circular groove which fits the edges of the slot (13) and is held in place by a spring bar (14). The groove secures even rotation of the central rod and prevents any longitudinal displacement, while the spring bar, owing to the square section of the rod, without preventing rotation, checks each quarter turn, the recognition of which is facilitated by the four arms of the cross-handle (12) at the top of the central rod, but is also shown unmistakably by the rotation of the whole inner cradle.

Precise rotation of the needle is thus well provided for and the measured projection of the concealed knife is effected by an arrangement in the inner cradle. This is traversed longitudinally by the central rod (11) which is fixed to both end plates (9, 10) so that they move together; the rod carries a sliding clamp (18) which resembles the screw stopper of certain bottles; its lower end is tapered, has a screw thread (22) and ring (21). The tapered end has a longitudinal slot (20) in front and by screwing the ring up the slot this is converted into a vice to grip the proximal end of the wire (19)

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which passes down the needle to the concealed knife (19). Near the upper end of the inner cradle the central rod is converted into a screw (16) for a few millimeters and a milled disc (17) works up and down it; the lower surface of the milled disc has a circular rim projecting from the circumference towards the center and fitting a corresponding groove in the upper end of the sliding clamp (18), permitting free rotation between the disc and the clamp. Owing to the square section of the central rod the clamp cannot rotate upon it, and the milled disc, when it is rotated and travels up and down the screw (16), carries the sliding clamp and therefore the wire and knife with it. The excursion is measured by an index (23) attached to the clamp and a millimeter scale (24), which is adjustable, attached to the adjacent edge of the inner cradle. As this scale is not visible when the cradle is rotated, it may be convenient to have another engraved on the adjoining edges of the disc and clamp, between (17) and (18), but it is doubtful whether this is necessary. In practice, the knife must be retracted till the end is flush with the opening in the needle at (30), and in this position the wire fixed in the slot (20) and the adjustable scale (24) set at zero; if this is done it is always easy to see whether the concealed knife is retracted and, if not, how far it projects.

Various needles of different sizes can be used with this bed; tapered hollow nozzles (25) of different sizes screw on to the lower face of the end plate (10) of the inner cradle, to engage the socket (26) of the needle. The socket has a slot (28) on the same side as the opening (30) at the end of the needle from which the concealed knife is projected and a small stud (27) on the nozzle engages this slot; it prevents slipping between the nozzle and the needle and indicates the direction in which the knife is projected.

Plates XVIII, XIX, XX, and XXI, show the application of the stage and needle in various positions to a cat's head fixed in the head-vice and cage.

Plate XVIII. Needle in first position above head. Vertical.

Plate XIX. Needle in first position above head. Needle inclined to left.

Plate XX. Stage and needle applied to left of cage, sixth position, needle inclined.

Plate XXI. Stage and needle applied to rear face of cage, seventh position, needle horizontal.

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CHAPTER V

ILLUSTRATED DESCRIPTIONS OF INSTRUMENTS (Continued)

Scales and Measurement of Movements of Needle, Gauging and Drilling, Methods and Applications, Charts and Microscopic Sections

A review of the preceding pages suggests that certain details, such as the measurement and corrections of the movements of the needle, which have appeared in different sections, might gain something in clearness if they were collected into a single description where they can be compared and studied together. This involves some repetition, but is preferable to ambiguity or obscurity in what purposes to be a laboratory guide rather than a book for the study. A student intending to use these instruments for experimental work needs to be familiar with all their details and on that ground may tolerate repetition which would otherwise be tedious, while, on the other hand, those who have found the preceding descriptions sufficient need not devote more attention to what follows than they consider desirable.

The scales of the needle appear confusing to those who are not familiar with them. One cause of this is that as the cost of the equatorial and indicator at present makes it difficult to bring the complete intrument within the reach of everyone, it is necessary to consult the convenience of those who purchase the cheaper form of rectilinear instrument to begin with and desire to procure the additional parts subsequently. For them it is a consideration that the same needle-holder should be available for both instruments, though the methods of measurement cannot be identical. There are some slight alterations in the pattern illustrated here which will be adopted in future and which it is advisable to explain.

Needle-Holder.—The holder now in use has been described (Chapter IV) and illustrated (Pls. XIV, XVI). Originally designed for the rectilinear machine, it was subsequently adapted for use with the indicator and has been lengthened since the illustration was prepared. It serves its purposes satisfactorily, but may be further simplified and improved by some trifling alterations. The movements and the

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methods of measuring and recording them, which depend upon the mechanism of the holder, are all connected with the projection of the needle. The other movements are effected by the equatorial (Pl. XXIX) or in the rectilinear machine by the two movements of the traversing stage (Pl. XIII). They are explained in the descriptions of the instruments referred to, but the essential points will be recapitulated here.

Equatorial.—In the equatorial (Pl. XXIX) the inner sheath (93) of the needle-holder fits and slides in an outer sheath (72) which is pivoted to the carrier (44), a slide block which travels on the arch (40) of the equatorial. With the projection of the needle from the holder, to be more fully described immediately, the arrangement practically affords universal movement. All movements of the equatorial, including projection of the needle, are measured by millimeter scales, the corrections required for variations in the size of different heads being effected by the indicator (Chapter VI) and explained in the description of it.

Rectilinear Machine.—In the rectilinear machine the longitudinal (91) and transverse (70*a*, 70*b*) guides of the traversing stage (Pl. XIII) afford two rectilinear movements in the plane of the stage perpendicular to the needle, the projection of which completes the movement in three dimensions. The outer sheath (72) of the holder is pivoted to the carrier (71) which travels on the guides, and a quadrant (77) provides for an inclination of the needle in one plane, the movement being directed and measured by an indicator. With inclined or universal movements so directed, if the same operating mechanism, whether it is the equatorial or the cage and stage, is applied first to the indicator and then to the head in the head-vice, no scales except those which measure the projection of the needle are required; for in the first of the positions, if the needle has been brought to a given point in the indicator, when it is transferred to the head-vice, it must reach the corresponding point in relation to the zero planes in the head, and the scales for projection of the needle are required only to allow of the retraction of the needle while the skull is trephined and its subsequent projection to the original position. But if duplicate instruments are used, one applied to the indicator and the other to the head, every movement performed by the first instrument must be precisely copied in the second and therefore all movements must be regulated by scales. To ensure identical move-

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ments in duplicate instruments, millimeter scales are sufficient. No correction for size is required, as it has already been effected in the indicator; therefore, for such movements proportional scales are never used.

Traversing Stage.—The measurement of the rectilinear movements of the traversing stage is simple. The millimeter scales engraved on the longitudinal and transverse guides have a zero near their middle and the scales are graduated on both sides of this point. Two lines drawn through these zero points parallel to the sides of the stage form a cross and when the stage is applied in any position above the cage (Pl. X), or behind it (Pl. XII), these crossed lines coincide with the crossed zero lines of a parallel lamella; *i. e.,* a horizontal lamella in the first case and a frontal lamella in the second. If the head in the machine were of standard size in both dimensions, it would obviously be easy to rack the needle the same number of millimeters from the crossed lines or zero points of the stage, as the objective is reckoned from the zero lines in the chart and in the assumed lamella of the head in the machine, and then project the needle till it reached the objective. But if the dimensions of the head in the machine are not of standard size the millimeter scales must be corrected to correspond with any variation, or proportional scales which have been set in accordance with previous measurement of the head must be employed.

Two Transverse Guides Differently Graduated.—If Plates XI and XII are compared it will be seen that in Plate XII the stage is applied to the rear face of the cage (position 7) in such a way that the zero in the middle of the transverse guide (70*b*) coincides with the upper surface of the horizontal frame or head-vice which is the level of the basal horizontal zero plane, but when the stage is applied to either side of the cage positions (5 or 6), as shown in Plate XI, owing to the position of the screw clamps and ear pivots attached to the lateral bars of the head-vice, the stage must be applied with its side resting on the horizontal frame and the zero in the middle of the transverse guide (70*b*) cannot be made level with the upper surface of the head-vice or the basal zero plane and therefore does not correspond with the basal zero plane in the chart or the head. For positions 5 and 6 another millimeter scale is engraved on the transverse guide (70*a*), graduated in millimeters from a zero level with the upper surface of the frame when the stage is applied as seen in Plate XI (position 5 or 6). This guide (70*a*) is marked *Trans.*, indicating that this

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scale is used for vertical measurement when the needle is directed transversely, as it must be when applied to either side. The same extensible scale is used for both guides (70*a* or 70*b*), but a spiral is selected for zero which corresponds with the zero engraved on the scale which is used. The same index reads both the engraved and extensible scales and, if desired, an ivory millimeter scale can be attached which can be read more easily than an engraved scale, but is not indispensable. The same index reads all three scales (see Plate XIII (81)).

Direction of Needle to Objective.—Any objective point must lie in one lamella at least in all three planes and can therefore be located in a chart in any of them. One of these planes is perpendicular to the needle, the other two parallel to it. If the objective is located in the first (perpendicular) lamella, the two movements of the stage bring the needle opposite the objective, and the third movement, the projection of the needle, directs it to the required point. If the objective is defined in a lamella parallel to the needle (and with the inclined needle this is necessary), one movement of the stage carries the needle to the edge of the lamella, as if it were the page of a book; the other movement of the stage and the projection of the needle bring it to the objective point, as if this were a given letter in a given line of that page.

Rectilinear Machine. Inclined Movement.—The quadrant attached to the stage provides for an inclination of the needle in one direction and one plane. If it is desired to introduce the needle obliquely it must be directed by an indicator, as described in Chapter VI. If a single operating mechanism is employed, the cage and stage with the needle must first be applied to the indicator, the needle set at any required angle and then directed by sight to the index point and all movable parts fixed. The point to which the needle is projected is noted on its scale; the needle is then retracted sufficiently to be out of the way and the cage and stage are applied to the head-vice which contains the head, the needle projected till it touches the surface of the skull, the point marked and the cage removed while the skull is trephined. The cage is then replaced and the needle racked through the brain till the index reaches the point noted on the scale when the needle arrives at the objective point in the brain. Or, duplicate operating instruments may be employed. An indicator, in which the essential parts of the operating mechanism are reproduced, is required;

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a finder needle, representing the operating needle, is set at a given angle and directed by sight with two movements to the index point corresponding to the objective. By similar scales the movements of the indicator are copied in the operating machine and the needle brought to the objective in the brain. As the inclination of the needle and the objective are in the same plane, besides the inclination of the needle, two movements and a two-dimensioned indicator are sufficient. One movement of the stage brings the needle to the edge of a lamella in the same plane as its own inclination, the second movement of the stage and the projection of the needle are sufficient to direct it to the objective.

Proportional Scales.—It is important to note that in this proceedding a proportional scale or correction for variation in the size of the selected head is required for the first movement of the stage which brings the needle to the edge of the lamella, but for the two remaining movements, *viz.*, the second movement of the stage and the projection of the needle which are directed by the indicator, a proportional scale is not employed, as any correction required must be made in the indicator.

When the indicator is employed with duplicate instruments, movements are directed by sight in one and merely copied in the other; or, if the operating instrument is first applied to the indicator and then to the head, the only scale required is that which shows the projection of the needle, and for this, one mark would suffice to indicate the point reached in the indicator, so that the original position could be regained after the needle had been retracted for trephining the skull. In rectilinear movements, and in these only, the position of any point in the brain in relation to the zero planes is ascertained in the chart and directly measured in the brain by the scales of the instrument. The distance of an anatomically identical point from a zero plane in two heads of the same species of animal is not necessarily the same, but roughly proportional to the size of the given dimension of the heads; therefore, whenever the scales of the instrument are used to measure a point in the brain from a zero plane in accordance with a chart, proportional scales or correction are necessary, but measurements of movements of the instrument for comparison; or of the length of the needle, are not affected by the size of the head and are always recorded in millimeters.

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In the instance just explained in which an inclined needle is directed to an objective point in the brain, the distance of the required lamella from the parallel zero plane, which is measured by the scale for the first movement of the stage, depends upon the size of the selected head, hence a proportional scale or correction is required; but with the other two movements, to copy a duplicate instrument or project a needle a given distance, a millimeter scale is sufficient. Obviously, if the inclination of the needle is not required, it can be directed to the objective by three rectilinear movements, two of the stage and its own projection. Each of these movements depends on the distance of a given point in the cranium from one of the zero planes; ascertained in the chart and measured by the scales of the machine in the selected head, in each case the distance depends upon the size of the respective dimensions of the head, and proportional scales or corrections are necessary in all of them. The cage and stage together are the counterpart of the equatorial, with a more limited range restricted to rectilinear movement in three planes and one inclined in one direction and in one plane, while in the equatorial the movements are universal. On the other hand, the former can be directed and measured by the scales of the instrument or by an indicator, while with the latter an indicator is indispensable. In either case, when the indicator is employed, the same mechanism can be applied first to the indicator and then to the head, in which case no scales but that for the projection of the needle are required. Or, duplicate instruments can be applied to the indicator and the head, all movements in the first being copied by corresponding scales in the second. Two of the three dimensional movements provided for the needle in the rectilinear instrument, effected by racking the carrier (Pl. XIII, 71) on the longitudinal and transverse guides (70, 91) of the stage, having been explained, the third, the projection of the needle perpendicular to the stage, now requires consideration. It is necessary, for reasons which have been stated, that the same needle-holder should be available for use with both the rectilinear machine and the equatorial, and as it is not practicable to adopt the same method of measuring the excursion of the needle in these instruments, two sets of scales on the same holder are required which appear confusing until they are understood.

Measurement of Projection of Needle.—In the rectilinear machine measurements are made directly from the central zero planes of the cranium which coincide with the zero points of the instrument; all

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scales are graduated from these points to show the distance of the needle from them. Scales for rectilinear projection register the distance of the point of the needle from the zero plane to which it is perpendicular, and when the index reaches zero on the scale, the point of the needle is at that zero plane. With the equatorial, or any needle inclined at various angles, it is not practicable to indicate the distance of the point from central zero planes in this way. Another instrument, the indicator, is employed, in which the needle is directed by sight to a point representing the objective, and the movements are identical with those in the operating instrument in which they are repeated by corresponding scales. Here the scales for the projection of the needle are required only to ensure correspondence of the duplicate instruments and that the needle is projected the same distance in both, its length being measured in millimeters from the point to the pivot on which it is inclined. Thus we have a scale for rectilinear movements, on the right, which records the distance of the point of the needle from the zero plane to which it is perpendicular, and the indicator scales for inclined movements, on the left, showing the length of needle projected from point to pivot.

Single and Separate Scales.—Whether they are rectilinear or inclined, two projection movements are provided: one, a coarse adjustment, by sliding between the sheaths; the other, or fine adjustment, by racking the bed with the needle in the inner sheath; and they can both be recorded on the same, or on separate scales. Each method has certain advantages. A single scale is more simple, and as different scales are required, in any case, for rectilinear and inclined movements and it is not desirable to increase their number, for an instrument of the present size, large enough for a full-sized rhesus monkey, the single scale is preferable. To meet every possible inclined position, however, the scale should be about 9 cm. long for the rhesus or a good deal more for larger heads, and this might be inconvenient; hence, the details of both methods should be considered. In the needle-holder shown in Plate XIV which was gradually evolved with the instrument, both methods are illustrated, separate scales being employed for rectilinear movements, on the right, and a single one, for the inclined needle, on the left. For descriptive purposes it is convenient that both methods should be illustrated, but for the future, whichever is selected, it will be better to adopt the same on both sides.

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A distinction to be specially remembered between the rectilinear and inclined scales is that, with the former, the distance of the objective, or any point in the cranium, from the zero planes is directly measured by the scales and, therefore, as heads vary in size, the measurements must be proportional, if they are to correspond with the charts. The engraved scales of the instrument are in millimeters, which are only applicable to heads of standard size; for others, corrections must be made or proportional scales introduced; the latter method is more convenient and one of the extensible scales described (Pl. IX, Chapter IV) is attached to the millimeter scale (Pl. XIV, 112) and both are read by the same index, which thus records the distance of the needle from the zero plane in millimeters and coordinates proportional to the size of the head. The scale of the inclined needle (110), on the left, is not employed for direct measurements of the cranium; these have been made and corrected in the indicator, the movements of which are exactly repeated in the operating instrument, for which purpose it is sufficient to know the length of needle projected, from point to pivot, in millimeters and be sure that it is the same in both instruments.

Adjustable Index.—Another detail is the adjustable index which is required with both scales if glass needles are used. As the point of the needle is a base of measurement in both methods, its position in precisely defined relation to the index is important and the needle must be exactly the right length or its index adjustable. If a glass needle happens to break in the course of an operation and a new one is substituted quickly, it is difficult to secure absolute accuracy and much more convenient to use an adjustable index which within certain limits can be adapted to a needle of any length. Such an index is, therefore, provided on both sides.

The details of the various scales for directing and measuring the projection of the needle which have been referred to will be considered under the following heads:

1. To begin with, a summary of the requirements which are essential in a needle-holder intended to direct and measure the projection of the needle with the rectilinear instrument or the equatorial.

2. An explanation of the way these requirements are provided for in the present holder (Pl. XIV).

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3. A short description of alternative methods of registering rectilinear or inclined movements with coarse and fine projection which are recorded on a single or on separate scales.

4. The pattern recommended for the future.

1, a. The first requirement is an arrangement of scales, by which the same needle-holder will serve for the two methods of measurements employed with the rectilinear instrument and the indicator.

1, b. Secondly, each scale must be provided with an adjustable index to correct differences in the length of needles, especially of glass ones.

1, c. Thirdly, in each case, two extension movements of the needle are required: (1) A coarse adjustment, effected by sliding the inner in the outer sheath, to bring the stop up to the skull; and (2) a rack and pinion extension for projecting the needle into the brain. These two movements can be registered by a single scale and index, or two; the former has the advantage of simplicity, but the mechanism for the latter is more compact.

1, d. Lastly, if extensible scales are used for making corrections for size, they are required only for rectilinear measurements of the cranium and must be attached to the scale which records them.

Next, to explain how these requirement are provided for in the holder which is shown in the illustration.

Needle-Holder.—In the needle now used and shown in Plate XIV the scales for the rectilinear instrument are on the right; the coarse and the fine rectilinear projection are directed and measured by two scales: (1) *The scale of the stop* and (2) *the scale of the needle.* The former registers the sliding movement between the sheaths by a scale and arrow on the adjoining borders of the inner and outer sheaths on the right of the holder (See Pl. XXIX, 72, 93). The latter, the excursion of the needle through the stop effected by racking the bed in the inner sheath. This movement is recorded by an adjustable index (113) attached to the right edge of the bed and a millimeter (112) and extensible (111) scale fixed to the inner sheath. With rectilinear projection the scales record the distance of the stop or the point of the needle from the zero plane to which the needle is perpendicular. The stop being the termination of the inner sheath, sliding between the sheaths, carries the stop and needle to and from the zero plane; the stop and the zero points which define the zero planes are parts of the instruments and therefore constants, for the measure-

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ment of which no proportional scale is required. An arrow on the side of the inner (93) and a millimeter scale on the adjoining border of the outer sheath (Pl. XXIX, 72) show the distance of the point of the stop from the zero plane, and when the arrow reaches zero on the scale, the stop is at the zero plane. In practice, however, the stop cannot go beyond the surface of the brain; hence, the scale need not be graduated to zero, but not more than 10 millimeters can be dispensed with in case it might be required to reach the surface of the cerebellum in small animals. To give the needle as much support as possible, the stop is pushed into contact with the surface of the brain by its sliding movement and fixed with the screw (96). The scale of the stop on the outer sheath is then read by the arrow showing the number of millimeters from the stop to the zero plane. The objective is reached by racking the needle through the brain and the excursion recorded by the adjustable index on the bed and the scales on the inner sheath. The stop having reached the surface of the brain, its share of the movement is over, the rest is effected by the needle, the scale of which must be set to correspond with that of the stop. The first step is to make the point of the needle level with that of the stop, a position easily recognized by sight or touch; the distance from the stop to the zero plane in millimeters is known and the adjustable index is set at the same figure on the millimeter scale of the needle. An extensible scale, (111) previously set in accordance with the measurement of the head, is fixed in clamps besides the millimeter scale so that their zero points coincide, the index reads them simultaneously and as it is racked in, continues to indicate the number of millimeters and coordinates between the point of the needle and the zero plane; and when this is reached, the index is at zero on both scales. As it may sometimes be necessary to project the needle beyond the zero plane, the scale of the needle is graduated for 10 mm. below zero.

Extensible Scales.—It will be noted in this description that an extensible scale is employed with the scale of the needle, but not with that of the stop; the selection of these scales presents some difficulty to the beginner and must be made as clear as possible. An extensible scale is not required with the scale of the stop because the stop and the zero points are constants of the instrument, unaffected by variations in the size of the head; the scale is required to show the distance from the stop to the zero plane of the head, but as this coincides with

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the zero plane of the instrument, it is a constant also; there is no question of proportional variation; it is a direct measurement of the instrument expressed in millimeters and recorded by permanent scales.

When the stop has reached the surface of the brain and its excursion is ended, by setting the adjustable index on the scale of the needle, the latter is made identical with the stop and the scales continuous, so that the separate scales are united to form a single one which registers the whole excursion of the stop and needle without a break. It indicates the distance of the needle substituted for the stop from the same zero plane; these points are still constants and so far there is no question of proportional measurement. But now a new factor is introduced; the needle must be directed to an objective in the brain, the distance of which from the zero plane has been ascertained in divisions of the scale of the chart and these are coordinates proportional to the size of the head represented. Since the size of the head in the machine is also variable and the corresponding point cannot be found by measuring an equal number of millimeters, it is necessary to use a scale, the divisions of which have been corrected for size like those of the chart, or a millimeter scale corrected by calculation. The proportional scale is most convenient; the needle can be racked till its index records the same number of divisions of that scale from zero as have been counted from the zero plane on the scale of the chart. Here the distance of the objective point in the brain from the zero plane, which varies with the size of the head, is directly measured by the needle and a proportional scale is required. It is only with the rectilinear scale that the distance of a point in the brain from the zero plane, which varies with the size of the head, is directly measured by the needle in this way, and therefore it is only with the rectilinear scale of the needle that a proportional scale is required; with all others the measurements are in millimeters. This has been explained in the case of the rectilinear scale of the stop, and the indicator scales on the left record only the length of the stop or needle projected from the pivot. These are parts of the instrument; they are not required to measure a variable point dependent on the size of the head and they are always measured by millimeter scales.

Indicator Scale.—In the illustration (Pl. XIV) it will be seen that with inclined movements both coarse and fine projection of the needle are recorded on a single scale, which is engraved on the left side of the bed (110) and read by an adjustable index (Pl. XIII, 79)

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attached to the outer sheath. To provide for all oblique movements of the needle in the head of a large rhesus the scale should be 9 cm. long (it has been lengthened in the holder represented, since the plate was prepared). The scale of the stop is abolished, both the sliding movement between the sheaths and the racked projection of the needle being recorded on the millimeter scale (110) which shows the length of both stop and needle projected from the center of the pivot in millimeters.

The essential difference between the *rectilinear* and *indicator scales* is that the former are required to show the distance of the point of the needle or stop in any position from the zero plane to which they are perpendicular, while the latter record the length of needle or stop projected from the pivot; consequently, with rectilinear scales the projection is towards zero and the index travels down a descending scale, whereas with the indicator scales the movement begins at zero when the needle and stop are level with the center of the pivot, and the projection of either stop or needle carries the index up an ascending scale of figures. All inclined movements are recorded in millimeters and an extensible scale is not required.

Adjustable Index.—An adjustable index is required for needles of variable length and must be set at the outset as follows: The needle is racked down till its point is level with that of the stop, which is then brought opposite the center of the pivot by sliding the inner sheath till the *P. S.* line on the back of it is level with the top of the outer sheath and the index is set at zero on the scale. In practice, the stop is then moved into contact with the surface of the brain by sliding the inner in the outer sheath; here it is fixed and the needle racked through the stop and brain till it reaches the objective. Both movements are recorded on the same scale, the index showing the total length of needle projected—differing from the rectilinear scales where the index starts at the maximum figure, which is reduced by the excursion of the stop, leaving the remainder to be effected by the racked movement of the needle. It appears rather an arbitrary arrangement that with the rectilinear scale of the needle on the right the scale should be attached to the inner sheath and the adjustable index to the bed, while on the left the scale is on the bed and the index attached to the outer sheath. This is merely a matter of mechanical convenience; the milled head which racks the bed in the inner sheath must be on one side or the other. Here it is on the right, it occupies some space,

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and on that side it is more convenient to attach the adjustable index to the bed; on the other side, where the whole length of the bed is free, it is preferable to have the scale engraved on it.

Single and Separate Scales.—It will be desirable in future, whether coarse and fine projection are recorded on a single or separate scales, to adopt the same method on both sides—the single scale is preferable with small heads not larger than that of a rhesus. For larger ones, it will probably be more convenient to use separate scales. There are four methods of recording rectilinear and inclined movements with single or separate scales:

Rectilinear Movements. Right Side.	1. Coarse and fine projection recorded on a single scale.
	2. Coarse and fine projection recorded on separate scales.
Inclined Movements. Indicator Scales. Left Side.	3. Coarse and fine projection recorded on a single scale.
	4. Coarse and fine projection recorded on separate scales.

2 and 3 have been described; the arrangements for 1 and 4 are as follows:

1. Rectilinear Movements.—Coarse and fine projection recorded on a single scale. Right Side. Not shown in the illustration:

An adjustable index is attached to the right side of the bed. A millimeter scale, 9 cm. long with an extensible scale beside it, is fixed to the outer sheath, so that their zero points coincide. Both scales are read by the same index. The zero is central, *i. e.*, towards the point of the needle, so that, as this is projected, the index travels down a descending scale and is at zero on both scales when the needle reaches the zero plane to which it is perpendicular. The adjustable index is set at the outset as follows: The distance from all surfaces of the cage to the parallel zero plane is the same, so that in any position of the stage the distance of a fixed point, such as the center of the pivot of the outer sheath from the zero plane which is perpendicular to the needle, is a constant, *viz.*, 70 mm. We therefore make the point of the needle coincide with that of the stop and the latter level with the center of the pivot by bringing the top of the outer sheath to the *P. S.* line of the inner sheath and set the adjustable index at 70 on the millimeter scale. The point of the needle is therefore 70 mm. from the zero plane and, as either stop or needle is pro-

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jected, the index shows the number of millimeters between the point of the needle and the zero plane, and at the same time the equivalent number of coordinates on the extensible scale which is set in accordance with the measurement of the selected dimension of the head in the machine. The stop is pushed into contact with the surface of the brain, the number of divisions between the objective and the zero plane are noted in the chart, and the needle is racked to the same number of divisions of the extensible scale from zero, when the point of the needle will reach the objective. If an extensible scale is not available a millimeter scale can be used, but the number of millimeters from the zero plane to the objective must be corrected in proportion to any variation in the size of the dimension of the selected head from the standard.

4. Indicator Scale. Left Side. Separate Scales (not shown in the illustration). Here the sliding movement between the sheaths, coarse projection, is registered by the scale of the stop, a millimeter scale engraved on the left side of the outer sheath read by an arrow on the adjoining border of the inner sheath. While the racked projection of the needle through the stop is recorded by the scale of the needle, which is also a millimeter scale engraved on the left of the bed, it is read by an adjustable index attached to the inner sheath. The first of these scales indicates the distance of the point of the stop, and the second the point of the needle, from the center of the pivot. The two scales are coordinated and the adjustable index set in the same way as the separate rectilinear scales. The points of the stop and needle are made to coincide; the inner sheath is pushed in until the stop is in contact with the surface of the brain, and fixed, the number of millimeters it is projected from the pivot is read on the scale of the stop and the adjustable index set at the same figure on the scale of the needle. In both scales the index traverses an ascending scale of figures beginning with zero, and as the needle is racked through the brain, it continues the scale from the point where the scale of the stop terminated and so registers the total projection of the stop and needle from the pivot. It is not necessary that the scale of the needle should be graduated below 20, as the stop must always travel that distance from the pivot to reach the skull; the length of the scale of the needle is therefore diminished to that extent. As both scales are required to show the length of needle and stop projected from the pivot, and as this is an intrinsic measurement of the

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instrument, all records are in millimeters and no proportional scale is required.

Summary.—In the preceding description the details to be specially noted are the following:

The rectilinear scales show the distance of the stop or needle from the zero plane; the indicator scales, the distance of the same points from the pivot. Both these are measurements of the instrument and could be recorded in millimeters. But the rectilinear scales of the needle are also required to identify the position of the objective point in the brain by indicating its distance from the zero plane in terms of the chart where the nominal millimeters are coordinates. Therefore, this distance must be recorded not in millimeters, unless the dimension involved is of standard size, but in coordinates or corrected millimeters, proportional to the size of the dimension compared with the standard. If the correction is made by calculation, a millimeter scale can be used; otherwise, an extensible scale is necessary.

Lastly, the adjustable index must be set to correspond with some constant. With separate scales on both sides the coarse projection is recorded by the scale of the stop. Here the sliding movement between the sheaths is completed before the index of the needle is set; then, the needle and stop having been made to coincide, the adjustable index is set at the same figure on the scale of the needle as the arrow shows on the scale of the stop; in other words, the scale of the needle is made a continuation of the scale of the stop. The constant in this case is the scale of the stop. With single scales, on both sides the scale of the stop is abolished. Both coarse and fine projection are recorded on the scale of the needle and the adjustable index must be set at the outset. The points of the stop and needle having been made to coincide, the stop is made level with the center of the pivot by bringing the *P. S.* line on the inner sheath to the top of the outer sheath. Then on the rectilinear scale the adjustable index is set at 70, on the indicator scale at zero. In the former, with any projection of either stop or needle, the approach to the zero plane is recorded towards zero on a descending scale; in the latter, similar movements are recorded from the pivot which is represented by zero on an ascending scale. The constant here is the pivot which is 70 mm. from the zero plane parallel to the stage and perpendicular to the needle.

The best pattern for the needle-holder in future appears to be one similar to that illustrated, but with an instrument suitable for heads

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not larger than that of a rhesus it will be advisable to employ single scales, 9 cm. long, for coarse and fine projection on both sides as described (1 and 3).

Gauging and Drilling. Methods and Application, Charts, Microscopic Section, Frontal Sinus in the Cat

In some respects it would have been advantageous to include the following description in the second chapter, as the topographical data, upon which operative procedure is founded, depend upon the accuracy of the methods of measurement, and some knowledge of these methods is required for a complete estimate of the topographical principles and their application.

But, as the instruments employed for gauging and drilling are attached to the head-vice and cage, it was necessary to describe the latter first and, having carried the description of the rectilinear instrument so far, it was undesirable to interrupt it with an account of the procedure, which will now be explained.

Gauges and Drills.—Accurate measurement of the cranium of a living animal is a matter of some difficulty; the method described here has gone through several modifications and has, I hope, reached somethink like finality. Not mathematical accuracy, which is impossible with such irregular and in some parts yielding structures, but it is probably as near it as the conditions permit; the unavoidable errors are small, the procedure simple and fairly quick and there should be no serious mistake.

Formerly, with the rectilinear machine, measurement of the cranium was effected by a depth gauge with a needle-point applied to the free surfaces of the cage. This is shown in Plates XXII, XXIII and XXIV. For drilling, a rectangular frame, carrying drill guides, was applied to the cage in three positions shown in Plates XXXI, XXXII and XXXIII. The procedure was simplified and improved in the combined gauging and drilling cage (Pl. XXXIV) which is more satisfactory for both purposes.

It may be objected that the special cage is cumbersome and some simpler instrument might serve the purpose; several have been tried without much success. All forms of calipers are untrustworthy, but the modified depth gauge with a needle and cap (Pl. XXII) answers the purpose, if care is taken to ensure its application to correspond-

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ing points in all cases. As a slight difference in the direction of a diameter may cause appreciable error, the needle must be perpendicular to the zero plane and in addition to this it requires a cage and cannot be used with the equatorial. So, for those who have already procured the rectilinear machine and the cage which belongs to it, this gauge may be recommended, but anyone who has the equatorial and would have to obtain a cage, as well as the needle gauge, had better obtain the combined drilling and gauging cage complete.

The same remarks apply to the matter of drilling. If it is resorted to only occasionally, the detachable frame (Pls. XXXI, XXXII, XXXIII) applied to the cage of the rectilinear machine will serve the purpose of those who have the latter instrument and save the expense of the special cage (Pl. XXXIV). Illustrations of this frame are given, but the special cage is much more satisfactory.

The Needle Gauge.—(Pls. XXII, XXIII, XXIV.) The illustrations and explanatory notes make a lengthy description of this gauge unnecessary and its application is further explained in the account of the measuring cage which follows; the only difference being that, instead of guides to direct a needle gauge permanently attached to six sides of a special cage, there is a needle gauge (136) mounted on a sliding joint (142) on a base bar (131), with two sliding feet (132) which can be applied to any surface of the ordinary cage of the rectilinear instrument.

The gauge shown in the illustrations was graduated for use with a cage in which the three diameters were different and the adjustable index (139) had to be set for each. There are two scales on the gauge. One (134) reading from the needle is employed only for setting the index; the other (135) is employed for measuring the cranium. The measurements on this scale are reckoned from the point of the cap (138) when it is screwed up (136); in this position, the point of the needle (137) is exactly flush with the point of the cap and therefore the point of the needle or of the cap serve as the zero of scale (135) read by the index (139). To set the gauge, the figures engraved on the foot (132) are required, the number selected depending on the dimension to be measured, *i. e.*, transverse, longitudinal or vertical. The index (142) is brought to the figure given on the foot (132) for the required diameter on the scale (134) and fixed with a screw not seen in the photograph; the index (139) is then set at zero on scale (135) and fixed with the screw (141). When it has been set

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in this way, if the gauge is applied to the cage in the required diameter, the point of the cap or needle will be at the zero plane to which it is perpendicular (Pl. XXII). If the screw which fixes the gauge is then relaxed and the gauge applied to a head in the cage (Pl. XXIV) and the needle made to penetrate the integuments to the bone, the index (139) shows on scale (135) the distance in millimeters from the zero plane to the surface of the bone. In the example shown, the object is to measure the vertical diameter of the cranium from the basal zero plane to the vertex. The figure given at (132) for the vertical diameter is 52, so the index (142) is brought to 52 on the scale (134) and fixed and the index (139) set at zero on the scale (135). If the gauge is then applied to the cage so that the needle is directly over the point where the sagittal and frontal zero planes intersect, the point of the needle will be at the interaural line (Pl. XXIII). The fixing screw is relaxed and the sliding gauge (136) withdrawn sufficiently to apply it to the head in the cage (as shown in Pl. XXIV), the needle is pushed through the integuments up to the bone and the index (139) is seen to be at 30 on the scale (135). The distance from the basal zero plane to the vertex at the selected point is, therefore, 30 mm. in this head. In future, with a cage in which the three diameters are identical, it will not be necessary to set the gauge for any diameter—the adjustable index and second scale will not be required. It will only be necessary to apply the gauge to the head (as in Pl. XXIV) and the index (142) will show on a single scale on the sliding gauge the distance of the surface of the bone from the zero plane in any diameter.

Drilling.—The use of the drill has been explained in the account of the preparation of chart sections in the first part of the atlas and will be described again in this chapter. In all sections of the cranium in any plane, the position of the other two zero planes is indicated by crossed lines and these are defined by three drill punctures in a line, the drill being perpendicular to the plane of section. The central puncture is made at the intersection of two zero planes; the others 10 mm. on each side of it. A line connecting the three punctures represents one of the zero planes in section and a second line through the central puncture, at right-angles to the first, represents the other. It is desirable that a drilling apparatus should be available, as the only charts published at present are those of the cat. The first part of the rhesus is issued with this description, but if any other species of ani-

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mal is used for investigation, the experimenter must prepare his own charts; not necessarily a series, a few sections may suffice, but these must be prepared in the usual way. For topographical purposes, also, such as the localization of a lesion, a drill is often useful and lastly, although, with care, accurate measurements can be made with a needle gauge applied to the ordinary cage, it is more satisfactory to make them with the special apparatus.

Gauging and Drilling Cage.—(Pl. XXXIV.) Of the two purposes of this instrument, drilling requires most attention, as it presents greater difficulties; and while a drilling cage can always be adapted for gauging, the converse may not be true, as an efficient gauging instrument might not be rigid enough for the drill. Gauging, however, must be practised in living as well as in dead animals, whereas drilling is, of course, only employed with the latter, and, as a rule, with heads which have been separated from the body. With a rigid frame and adjustable guides, regulated by scales, the drill is directed through the cranium in any of its three diameters. Three punctures are made in a line at measured intervals, in the zero planes which they define, vertically and transversely in the frontal, and longitudinally in the horizontal zero plane. To define the zero planes accurately the head must be adjusted in the head-vice, to which a cubical skeleton frame, similar to the cage of the rectilinear machine, but stouter and heavier, is applied. It is provided with feet and bolts like the ordinary cage and engages the same slots, and adjustable drill guides in opposed pairs are fitted in slide blocks (5, 6, 17, 18, 23, 23) to the six sides of this cage. The drill guides proper (7, 8), as distinguished from the slide blocks which carry them, are cylindrical rods 6 mm. in diameter, bored in their long axis for the drill and themselves fitting cylindrical slots in the slide blocks which travel on the graduated guides (1, 2, 3, 4, 15, 16) of the cage. The movements of the slide blocks are regulated and any pair of them can be accurately adjusted, at opposite points of a selected zero plane, by the scales on the traversing guides, and the blocks can be fixed in any position with screws. The cylindrical drill guides also slide in their slots and can be pushed into firm contact with the cranium and fixed with screws, the object being to give the drill as much support as possible and especially to prevent it from slipping, where it engages an oblique surface of bone. The drill is introduced first on one side of the head

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and then on the other and then a long needle (32) is passed through the cranium from guide to guide.

The traversing guides, which carry the slide blocks and drill guides, are fitted to the cage as follows: Four bars (1, 2, 3, 4) graduated in millimeters and each carrying a slide block (5, 6, 23, 23) form a rectangular frame, which is fixed over the cage in the frontal plane just in front of the frontal zero plane, so that the centers of the slots of the slide blocks coincide with the zero plane above, below and on both sides. This frame is permanently fixed to the cage and, in order that the latter may be lowered over the head, the inferior guide (4) of the drilling frame is detachable. The other three sides of the frame are fixed astride the cage, which is applied from above over the head; four feet with bolts (67, 68) fit the slots of the head-vice and are firmly locked. The lower detachable guide terminates at both sides in joints (13, 14) which fit over the extremities of the vertical guides (2, 3) of the frame and are fixed with screws, thus completing the quadrilateral frame for vertical and transverse drilling. For the former, the upper and lower slide blocks are brought to zero, which is the middle point of the transverse guides, and in this position the centers of the drill guides coincide with the intersection of the sagittal and frontal zero planes. The head is drilled here, and this is the center of the three vertical punctures; the slide blocks are than moved successively 10 mm. on both sides of this point and the drilling repeated, completing the three vertical punctures in the frontal zero plane. For transverse drilling in the same zero plane, the lowest of three punctures in a vertical line is made through the ear pivots, which are bored for this purpose (31, 31); the next puncture is made through the drill guide at the level of the horizontal zero plane; and the third at the same distance above the second. The mid-horizontal zero plane is not a constant, being one-third of the distance from the meatus to the vertex in the cat and one-fourth of that distance in the monkey. The punctures are made at corresponding intervals by the adjustment of the slide blocks on the scales of the vertical guides of the frame. As this drilling frame is fixed in the frontal zero plane, which is a constant, no longitudinal adjustment is necessary. A single movement on the transverse guides for vertical drilling and on the vertical guides for transverse drilling is sufficient to bring the drill to any of the points indicated. But, as longitudinal drilling is practised in the mid-horizontal zero plane, which is not a constant, both vertical and

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transverse adjustments of the slide blocks (17, 18) are required. For this purpose the anterior and posterior transverse guides (15, 16), which carry the slide blocks of the longitudinal drill guides, terminate at both ends in joints (21, 21, 22, 22) which slide vertically on the anterior and posterior pairs of legs (Pl. X, 65, 65, 66, 66) of the cage, and they can be raised or lowered and fixed with screws at any height on the legs which are graduated with millimeter scales. By this arrangement the anterior and posterior drill guides are brought to the same level and accurately opposed, first in the median sagittal plane and then at corresponding points 10 mm. to right and left of it.

Drills.—The drills, employed in the manner described, should be tempered and of about No. 14 standard wire gauge, 1.8 mm. in diameter; this is the smallest size which possesses sufficient rigidity for drilling a cranium as large as that of a rhesus monkey and would not be rigid enough for a larger head. Different forms of cutting points have been tried, the awl point, triangular in section, appearing to be the most satisfactory, although, theoretically, it is not a good form of drill, as it has no clearance or cutting edge; nevertheless, it penetrates the skull and its point is less easily deflected by an oblique surface of bone or membrane than more orthodox forms. When any form of drill engages such an oblique surface it should be run with light pressure and as rapidly as possible; a motor should be used if it is available, but an ordinary hand drill will generally give satisfactory results.

Preparation of Microscopic Sections.—It has been mentioned that the drill is chiefly used for identifying the zero planes in chart sections, and that anyone may have occasion to use it for that purpose. Drill marks are sometimes useful, especially for beginners, to assist in the localization of lesions and the identification of structures in microscopic sections. Most of us have wasted time and trouble in acquiring this accomplishment under difficulties owing to the capricious selection of planes of section and it is to be hoped that the adoption of constant planes in the charts will help to abolish such a gratuitous infliction. The following procedure is recommended for the topographical purposes referred to:

As a preliminary, the brain must be injected. A cannula is introduced into the thoracic aorta, the right side of the heart opened and a warm solution of 5 per cent formalin and 2 per cent potassium bichromate injected from a bottle raised from 1 to 2 meters.

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It is advisable to introduce ear cones before the injection, as with formalin the meatus becomes rigid. The head is then adjusted in the frame and the drill is applied in the cage in the zero plane perpendicular to that in which the sections are to be made, so that the punctures will appear as points in every section. This zero plane, and the one at right-angles to it, will be represented in every section by crossed lines. One of the punctures should be at the point of intersection and the two others 10 mm. on each side of it. If these punctures are visible in a section, by applying a glass plate with crossed lines ruled on it in such a way that the intersection coincides with the middle puncture and the other two points with one of the lines, the distance of any point in the section from the two zero planes represented by these lines can be estimated. To measure the objective point from the third zero plane, the sections must be made in accordance with that object. To effect this, in addition to drilling perpendicular to the plane of section, the zero plane parallel to the sections must be marked by two drill punctures, on each side which penetrate far enough to be seen on the surface of the brain, so that it can be cut accurately in this plane. After it has been hardened and the bone removed, the brain is divided in the zero plane marked by the punctures. Each half is then placed with the cut surface on a glass plate and the measurement of the dimension, from the zero plane to the surface, taken with a depth gauge. In cutting the sections, the division into lamellæ must be observed and the sections numbered accordingly. This object may be carried out in various ways. In the first place, the brain may be embedded in gelatine, 15 per cent, and glycerine, 5 per cent, and frozen, or it may be embedded and cut in celloidin; but in either case it must be divided into the correct number of lamellæ for the dimension by a proportional scale, after deducting the average thickness of the skull at that part of the cranium. One method is to fit the proportional scale to the microtome, an index recording the the movement of the knife (or the object) on the spirals of the scale; the spring may be included in a circuit and a brush contact with the spirals arranged to indicate by a signal each lamella as it is cut. Or, if preferred, the brain may be cut in the macrotome into proportional slices approximately 2 mm. thick. Here an index and proportional scale register the movement of the plate of the macrotome, each slice representing two lamellæ. When the sections are mounted, the slides are marked with the number of the lamella and section, which gives

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one of the measurements required for localizing any given point in the section. The other two are found approximately, and sufficiently accurately for practical purposes, by applying a glass plate, ruled in square millimeters to the slide, guided by the punctures which have been made in the section.

It may be observed that two punctures, one at the point of intersection and one 10 mm. from it on one of the zero lines, are sufficient for the correct application of the ruled glass plate, but three punctures are preferable, because one is sometimes missing, as, for instance, when it falls in a space between the hemispheres. But two out of three are generally visible and, as they are 10 mm. apart, any two suffice for the application of the plate and the restoration of the missing puncture.

Gauging.—The slide blocks, perforated with cylindrical slots for the drill guides and provided with a graduated adjustment on the traversing guides of the cage, are equally well adapted for measurement of the cranium with the needle gauge. The pattern of this gauge (Pl. XXXIV, 26), used with the drilling frame, is a cylindrical tube, 6 mm. in diameter, which fits the slots in the slide blocks. The slots are guides for the gauge and their outer margins are the indices which read the graduations engraved upon its surface. A cylindrical rod, carrying a needle at one end and a milled head (28) at the other, fits the tube of the gauge. The needle projects from one end and, at the other, a screw thread extends a short distance from the milled head, engaging a corresponding screw at the end of the tube so that by rotating the head of the rod, the needle can be projected from the tube or withdrawn. A perforated cap (27) tapering to a blunt point fits over the needle and is screwed on to the tube like the point of a pencil-case; when screwed home, the point of the cap is a constant from which the gauge is graduated. The needle can be projected through the cap or made exactly flush with it, in which case the measurements on the scale from the point of the needle and the cap are identical and the point of the cap or, when it is removed, the sharp point of the needle can be used indifferently for gauging. The tube is graduated with a millimeter scale, reckoned from a zero near the distal end towards the point of the needle or cap. As in the cage of the rectilinear machine, all the diameters, from any external surface or bounding plane of the measuring cage, to the zero plane parallel to it, are identical, vertically, transversely and longitudinally, and

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when the gauge is projected through any slot from outside, till the zero mark is level with the index, *i. e.*, the outer margin of the slot, the point of the needle, or cap, is at the zero plane to which the gauge is perpendicular and this distance is always 85 mm. As the gauge is withdrawn the index shows the number of millimeters from the point of the needle to the zero plane, so, if the gauge is introduced till the point of the needle touches the cranium, after penetrating the soft tissues, the index shows the distance in millimeters of the surface of the bone at that point from the zero plane; this is one of the required dimensions which is thus determined quickly and accurately. It is advisable that measurements should always be made with the bare needle to the surface of the bone; the puncture of the skin in an anæsthetized animal is negligible and in the occipital region, especially in cats, the thickness of hair, skin and muscles is considerable and variable. With this instrument, the cranial measurements, from the zero planes to the surface of the bone, can be made rapidly at the same points, ensuring constant diameters, and the direction of the gauge must be perpendicular to the zero plane—important details.

Selection of Diameters.—The vertical and transverse diameters of the frontal zero plane in the rhesus and cat are not quite the maximum diameters of the cranium, which are usually about 10 mm. further forward, but the difference is slight, not more than 1 or 2 mm., as a rule; the position of the absolute maximum is not quite constant, and it is doubtful whether varying the diameter, in order to secure the maximum, would afford a better guide to proportional dimensions than measurements through constant points, which are always near the maximum. It is more convenient that all measurements should be made at the same points, and on the whole, it seems best to adhere to the zero plane.

The same considerations apply to the mid-horizontal zero plane, which is the level adopted for drilling and gauging. The basal plane is quite unsuitable for these purposes, as it is too low. The mid-horizontal zero plane is the best level and about the maximum in the longitudinal dimension; the maximum transverse diameter is rather higher, but the explanation just given applies here.

Longitudinal Diameter in Rhesus.—In the rhesus the anterior longitudinal measurement is taken from the frontal zero plane to the glabella, the lowest part of the frontal lobes available. This is about 10 mm. above the horizontal zero plane, but as the measurement is

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between perpendiculars, parallel to the frontal plane, and the glabella is the most prominent point anteriorly, the exact level of this measurement is not material.

Frontal Sinus and Longitudinal Diameter in the Cat.—Owing to the large frontal sinus of the cat, the anterior limit of the brain cannot be defined from the outside in that animal. The anterior lobes are separated from the sinus by a thin plate of bone, about 1.5 mm. thick. This septum cannot be exposed without opening the sinus, which is therefore the only way to gauge the longitudinal diameter of the brain directly.

A puncture into the frontal sinus is a much simpler matter than one which penetrates the bone over the brain. It bleeds little, encounters no important structure immediately beneath it and can be expeditiously effected with one blade of the bone forceps. For animals not intended to survive the anæsthetic the direct measurement is the best. If a line connecting the posterior margins of the orbits is drawn transversely across the cranium, a puncture on it, through the frontal bone, about 5 mm. to one side of the sagittal zero plane, will give access to the anterior surface of the septum. The frontal lobes of the cat's brain are continued by the olfactory lobes in the form of a narrow prow or beak in the middle line. The bone which forms the septum is moulded over these structures and the most convenient point for measuring the anterior limit of the brain is at the angle where the root of this beak expands over the frontal lobes and which is about 4 mm. from the middle line. Having defined this, it may be measured from the front with the needle gauge or with a similar gauge (Pl. XXXIV, 34) which terminates in a small crossbar in place of the needle and which is intended either for this direct measurement or for that of the posterior margin of the orbit, which will be explained immediately. If the animal is to be kept alive, the contour of the septum can be felt with a probe through quite a small opening and the point described identified. In this case, after measurement, the sinus should be washed out with a 0.5 per cent solution of lysol and filled with boric acid. The septum is liable to some irregularity, and very rarely, and I think only in old animals, the whole sinus is filled with cancellous bone.

Although this procedure is not a serious addition to an operation, it would be more satisfactory to find a method of measuring the head without opening the sinus. It was pointed out in the atlas,

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that in the cases examined the distance from the interaural line to the septum and the posterior margin of the orbit was the same on the average, *viz.*, 31 mm. The measurements were taken in preparations after removal of the skin, but it is possible to make it in a living animal, and the screw rods on the mask (Pl. II, 12, 13) are used for this purpose. They terminate in rounded ends which bifurcate to form a cleft, the bottom of which is indicated by a small stud on one of the forked ends. When the mask is in position, the screw rods can be elongated till the cleft engages the posterior margin of the orbit about its center, the rod is projected by the screw till the bottom of the cleft is in moderately firm contact with the posterior margin of the orbit, indicated by the stud, which is kept outside, and can be measured with a depth gauge from the front of the cage. The modified needle gauge just referred to is now used both for measuring the posterior margins of the orbits and the frontal septum from the front of the cage, but the rods can be employed for the purpose, so that it was not worth while to alter the figures which show them. Any method at present is only provisional and it will require more experience before we can decide whether the relations of the septum to the posterior margins of the orbits are sufficiently constant to be adopted as an established method of measurement. It is not possible, therefore, to speak positively, but apparently in animals that are near the average size, and this generally means young adults, the measurement is fairly constant. With age the bones grow more than the brain and the indication is less trustworthy—one of the advantages of selecting animals of average size.

The plan I adopt is to measure the posterior margin of the orbit by the method described; if it is not more than 32 nor less than 30 mm. from the frontal zero plane, I accept it as the measurement of the septum. It is not often less than 30 mm., but if it is more than 32 mm., for the second and every additional millimeter in the orbital measurement I only allow half a millimeter for the septum.

Whenever the measurement of the septum has been estimated in this way, if possible, after the animal has been killed, the head should be put in the instrument and the septum measured directly with the depth gauge and the results compared. If this rule is followed by several workers, before long we shall have sufficient data to settle this question.

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It should be noted that the limits of this anterior frontal dimension are not of the same importance as the position of any of the zero planes from which direct measurements are made. It is only taken to estimate the relative size of that dimension compared with the standard, for the adjustment of the extensible scale. If there is an error, its extent depends on the distance of the objective point from the frontal zero plane. Thus an error of 1 mm. in the measurement of the dimension will amount to only a third of that distance if the objective structure is 10 mm. in front of the zero plane. But if the anterior part of the caudate nucleus were the objective, the error would be greater. In such a case it is advisable to select an animal of average size or to make a direct measurement of the septum with the pilot needle, or with the gauge, in the way described.

In the bones forming the posterior margin of the orbit in the carnivora there is a gap filled by fibro-cartilage; with the amount of pressure required, which is not great, it does not yield enough to affect the measurement.

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CHAPTER VI

ILLUSTRATED DESCRIPTIONS OF INSTRUMENTS (Continued)

Indicators (Pls. XXV-XXVIII), Equatorial (Pls. XXIX, XXX), Adjustment of Scales, Quadrant Scales (Pl. XXVII)

The principal object of improvements in the mechanism of the stereotaxic instrument has been to secure as great a flexibility and range of movement of the operating needle as possible without sacrificing accuracy and rigidity. It is important that the operator should have a choice of routes from the surface to any point he wishes to reach in the brain; there may be tracts or other structures which it is desirable to avoid, and although the injury produced by the passage of the needle is comparatively slight, it should not be ignored, nor should the possibility of its contributing to the degeneration attributed to an intentional lesion be overlooked. Again, in stimulation experiments, owing to the tendency to "escape," valuable information for the correction of error may be acquired if the focal point is approached by different routes and any variations in the response are noted and compared. The difficulty of securing the above objects has been due to the necessity of combining qualities which are more or less antagonistic; the freer the movements the less easy it becomes to measure and record them. If we depend on scales attached to the instrument to direct the needle, its excursions must be rectilinear; at least I am not aware of any satisfactory method of registering inclined or universal movements by scales. Fortunately, there is no need of one, as it is improbable that any other method could serve the purpose better than the indicator, an instrument in which all the essential conditions presented by the head and the stereotaxic machine are exactly reproduced. An index point, representing the objective, is adjusted with identical relations to three index planes which correspond to the zero planes of the cranium. Four pillars are fixed to the floor of the indicator in such a position that slots, like those of the head-vice, with which they are provided, have similar relations with the index planes and consequently with the index point. Any mechanism, for directing the operating needle, which fits into the

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slots of the head-vice, can be applied to the corresponding slots of the indicator and must have identical relations to the zero planes, and any points at the same distance from them, in both instruments. A single operating mechanism can be employed and transferred from the indicator to the head-vice; or, duplicate instruments may be used with corresponding scales in which the movements are directed by sight in the one applied to the indicator and copied in the other; or finally, a needle may be directed in the indicator from a frame, which, without being a duplicate of the operating mechanism, reproduces its essential parts and movements and records the latter with corresponding scales. The operating mechanism in the rectilinear instrument consists of a cage and traversing stage carrying a needle, the cage being fitted to the slots of the head-vice and the needle directed by scales to the objective point. This mechanism can also be applied to the slots of the indicator, if required for inclined movements of the needle which cannot be directed by its scales. Another form of operating mechanism, which affords the needle universal movement, is the equatorial; it fits the corresponding slots in the head-vice, and the indicator by which all its movements are directed. Thus, if either the cage or the equatorial is applied to the slots of the indicator, the needle can be manipulated in view, by any available movement, in any direction, from various positions, till it reaches the index point, and if the mechanism is then transferred to the head-vice, the needle will be at the corresponding point in relation to the zero planes of the cranium; *i. e.*, at the objective point. It is a simple mechanical procedure requiring no anatomical knowledge and, with one exception, no alteration in the adjustment of any part of the mechanism, nor even the use of the scales. The exception will be apparent; to reach the objective point in the brain the needle must penetrate the skull, which is trephined for the purpose. The operating mechanism cannot, therefore, be applied to the head-vice with the needle fully projected; its extension must be adjustable and regulated by a scale. When the needle has reached the index point in the indicator the position on its scale is noted; it is retracted sufficiently to permit of the application of the cage or equatorial to the head and then projected till it touches the skull. This point is marked. The cage can be removed while the skull is trephined, then replaced, and the needle racked through the brain to the figure noted on the scale, when it will have reached the objective point.

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This method of using a single operating instrument, either cage or equatorial, and transferring it from the indicator to the head has the advantage of simplicity. No scales are necessary except the one which records the projection of the needle, and even accuracy of the instrument itself is not of vital importance; so long as the slots have identical relations to the index and objective points in both instruments, if the needle is brought to any selected point in one instrument, it must be in the corresponding position in the other. For the majority of experiments, therefore, this method will probably be preferred, but a larger field of operative procedure is opened by employing duplicate instruments, one of which is applied to the indicator, and the other to the head; every movement, regulated by corresponding scales, is directed by sight in the indicator and copied in the duplicate. Here accuracy in every detail of both instruments is indispensable, as well as care to observe that the readings of all corresponding scales are identical. It may be questioned whether any probable advantages can compensate for the obvious defects of this method, the sacrifice of simplicity and a considerable increase of trouble and expense. There are some very decided advantages, but, perhaps fortunately, they are associated more with probable developments of the methods in the future than with their immediate application. But, even now, with the forms of cutting needles which are described (Chapter IV, Pl. XVII) and without counting on others which may be designed, there are planned operations for isolating centers, or nuclei, or tracts of considerable size, which may be of great value. It would be very difficult to carry these out with a single instrument, but they may be accomplished in consecutive steps, directed by sight in one instrument, and copied in the other. It will, I believe, be practicable, by substituting fine steel bars for silk threads in the gratings, to reconstruct a reproduction of various structures of the brain upon the floor of the indicator; instead of one index point there may be many, connected by elastic threads representing tracts, or blood vessels, and models of nuclei may be introduced. The reconstructions would be permanent, but with movable needles carried by the steel gratings and the use of elastic threads, the whole reconstruction could be automatically adjusted in three dimensions for variations in size, and operations of some extent performed with precision. It is upon these lines that we may look for the application of the methods of surgery, but such developments

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are more or less speculative and, for the present, we may be content with the simplicity and convenience of a single instrument or, at any rate, resort to duplicates only for certain special investigations.

There is an application of this method, however, available at the present stage with either a single or duplicate instrument which deserves mention. It consists of the utilization of hardened brains as models in which planned operations are carried on in one instrument and copied by means of corresponding scales, etc., on the brain of another animal of the same species, fixed in an identical machine; or, the operation may be carried out by sight on the model and every movement noted on the scales or recorded. The head of a living animal can then be fixed in the same machine and every detail of the operation repeated. Brains hardened in formalin and bichromate shrink very little and if the brain selected for the model is very nearly the same size as that of the animal operated on, the proportions of structure or nuclei upon which the operation is performed will generally be very similar. The model must be marked before the bone is removed in the manner described in Chapter V, so that, after it is hardened, the zero planes can be readily identified. It is fixed in a holder supported on a universal joint on a pillar which can be screwed into the plate of the indicator; the model can then be adjusted and fixed so that its zero planes correspond with the white zero lines of the gratings and any desired operations can be carried out with equatorial and the cutting needles described. Then either repeated on a head in another instrument with another equatorial, or, the recorded movements of the needles can be repeated with the same equatorial and needles, transferred from the indicator to the instrument attached to the head of the selected animal. In both cases the needle is directed by the scales, which are adjusted to repeat the procedure in the operation on the model.

At the present time, it seems probable that we may obtain important information relating to the anatomical connections and the functions of large nuclei, and other structures, if their communications can be cut and they can be more or less completely isolated without mutilation. This may be effected by employing the finest hypodermic needles from which steel wires can be projected for cutting purposes.

It is a practicable operation with the instruments now available and is not a merely speculative suggestion.

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In the foregoing description of the principles of the indicator, I have assumed that the index point is correctly defined, by constant units of measurement, from three index planes which correspond to the zero planes of the charts and cranium, and in the simplest form of indicator the measurements are in millimeters, as they are in the rectilinear machine. But, as has been explained, in the charts the units are coordinates proportional to the dimensions of the heads selected for section; in order, therefore, that the index point should coincide with the objective in the head chosen for operation some means must be adopted to correct the measurements for variations of size. If millimeter scales are used, they must be corrected by calculation or tables, but a mechanical method of correction is much more convenient and has been adopted in the indicators which have been constructed and are shown in the illustrations (Pls. XXV, XXVI, XXVII). Millimeter scales, however, are cheaper and their employment on economical grounds may deserve consideration, especially if the corrections are made with a mechanical calculator which saves a certain amount of time and trouble.

It has been explained that, owing to the difference in cost, it was desirable to give descriptions of two patterns of the operating mechanism, the simpler form, with rectilinear movements and inclination of the needle in one plane, in each position, and the more elaborate equatorial, with a wider range of movements which are practically universal. Similar reasons require a corresponding variation in the patterns of indicator which may be selected, the choice of which may depend on questions of cost, the pattern of stereotaxic instrument employed, and the work for which it is required. The **three-dimensioned indicator**, with mechanical correction for variation of size, effected by adjustable gratings, is the best, but it is expensive; it is designed for use with the equatorial, with which the needle can be directed in any position and at any angle, but it serves equally well for directing the inclined movement in the rectilinear machine and so fulfils all purposes. If a cheap pattern is required, it is probably most satisfactory to use a modified form of the same instrument, in which a card ruled with square millimeters is substituted for the adjustable gratings, the corrections for size in three dimensions being made by tables or calculation. But, with the rectilinear instrument, as the inclination of the needle is possible only in one plane, a **two-dimensioned indicator** is sufficient. It represents all the movements

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of the needle in one plane and can be constructed with a ruled card and millimeter scales, which require correction; or, as described with the three-dimensioned pattern, corrections can be effected mechanically with a reticulated screen formed by crossed adjustable gratings. I have not had occasion to use either of the ruled card patterns, but their construction will be explained. In the general description of instruments in Chapter III a short account of the indicator is given which has, I hope, conveyed some idea of its principles of construction, which will now be described with the help of Plates XXV to XXVIII in more detail. The principle of the two- and three-dimensioned indicators is the same, but in the former two gratings only are employed, combined to form a reticulated screen, and the movements and inclination of the needle are all in one plane; whereas, in the latter, three gratings are used to define the index point and the needle can be directed from any position and inclined in any plane. It is not necessary to add very much to the account already given of the method of substituting a ruled card for the adjustable gratings in the three-dimensioned indicator; it has no advantage except on the score of expense and involves the correction of millimeter scales in three dimensions by calculation, which is objectionable. The following description will explain its construction:

The Three-Dimensioned Indicator with Ruled Card.—A horizontal oblong plate 90 x 70 mm., *i. e.*, rather larger than a horizontal lamella in the rhesus, is mounted on a vertical pillar, graduated in millimeters and raised or lowered in a socket by rack and pinion. Cards ruled with square millimeters can be fixed to the plate, each card being marked with a crossed longitudinal and transverse line, representing the sagittal and frontal zero lines of a horizontal lamella in the charts. These zero lines must correspond with marks on the plate, so that the position is constant. On the stand that carries the pillar and plate there are four corner columns, the upper surfaces of which are slotted to receive the bolts on the feet of the cage or equatorial; the slots have the same relations to the crossed lines on the card as those in the horizontal frame or head-vice (Pl. V) have to the interaural and frontal sagittal zero planes of the cranium. The columns are all the same height, the table is brought to the same level and at this point the scale on the pillar is marked zero; this, the level of the surface of the columns and slots, is the basal zero plane and, the point being marked, the table can be raised or lowered

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any required number of millimeters above or below it. Any square millimeter on the card, of given distance from the zero lines, can be identified and marked and, the plate being adjusted to the given height in relation to the basal zero, the marked square represents a cubic millimeter, the required distance in three dimensions from three index zero planes, which have the same relations to the slots of the corner columns of the indicator as the zero planes of the cranium to the slots of the head-vice. If the cage, or equatorial, with the needle mounted is applied to the slots of the indicator or head-vice and the needle is fixed in any position, it must have the same relation to the three zero planes in both instruments and consequently the same relation to any point at the same distance from them. We can, therefore, use either form of operating mechanism, *i. e.*, cage or equatorial, and fit it on the slots of the indicator, manœuver the needle from any available position, by any practicable movement, till the point touches the marked square on the card, the position is noted on the scale of the needle and all other movable parts fixed. The needle can now be retracted as far as may be convenient, the cage or equatorial transferred to the frame on the head, the skull trephined and the needle finally racked in to the figure noted on its scale, when it will arrive at the objective point in the brain. The measurements will have been in millimeters and assume a standard head; for variations in the size of a selected head in any of its three dimensions corrections must be made, with a mechanical calculator if preferred, both on the ruled card and the scale of the pillar.

The **three-dimensioned indicator** illustrated in the accompanying plates (XXVII, XXVIII) is constructed on the same principles as that just described, with the exception that the position of the index point is determined by three adjustable gratings instead of the millimeter scales of the card and pillar; the gratings are corrected for variations in the size of any selected head, in three dimensions, and as the position of the index point is determined by these gratings, it is varied in the same proportions and the measurements require no further correction.

Three adjustable gratings represent the three zero planes in longitudinal, transverse and vertical dimensions, and the index point is identified and measured from them by two needles, carried upon movable bars, so that they can be made to correspond with any divi-

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sions of the gratings. When they are adjusted, the point of intersection of the two needles is the given number of divisions or coordinates from the zeros of the gratings in three planes.

The longitudinal and transverse dimensions are represented and measured by two horizontal gratings, closely applied to one another at right-angles to form a single reticulated screen (Pl. XXVII, 4, 8, 12). The gratings are formed of silk threads, stretched between pegs on opposite pairs of sway bars (5, 9, 13) which can be adjusted at any angle within the limits of their movements. By graduated quadrants (6, 10, 14) and screws (7, 11, 15) they can be fixed in any position and the spaces between the threads regulated and measured. On one of each pair of sway bars a stretcher is applied to regulate the tension of the threads, which are divided by contrast colors into groups of five, so that they can be counted quickly. It will be seen that white threads pass between the centers of the pivots of opposite pairs of sway bars; these threads are not moved by inclining the bars and they represent the zeros from which measurements are made; in the horizontal screen, two of these threads represent the interaural and median sagittal zero lines. Two white threads on each side of the median sagittal line define the transverse dimensions of the standard cranium of the cat and rhesus monkey and when the quadrant scales are set at 40°, so that the divisions of the grating measure millimeters, these lines represent the transverse dimensions in standard animals. In the transverse gratings, similar white threads represent corresponding anterior and posterior measurements in the same animals.

Adjustment of Gratings.—The transverse grating is composed of two pairs of sway bars and consists of a prefrontal and postfrontal portion, each of which can be adjusted independently. This is necessary, because variations in these dimensions do not always correspond in the same cranium; the prefrontal dimension may be greater than the standard and the postfrontal less, or vice versa. When the quadrant scales are set at 40° the divisions measure millimeters in all gratings and each degree on the quadrant scales is equivalent to one-fortieth of a millimeter in every division of the gratings; consequently, the effect on a whole dimension, represented by a given number of threads, produced by moving the sway-bars one degree on the quadrant scale, depends on the number of divisions in the dimension. A dimension of 40 divisions is varied 1 mm. by a movement of one degree, one of

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20 divisions, half a millimeter, and so on; and if it is desired to vary a dimension a given number of millimeters, the proportion of that number of millimeters to degrees of the quadrant will be the same as the number of divisions of the dimension to 40. If the dimension has 20 divisions then 20:40:: number of millimeters: number of quadrant degrees. The gratings can be adjusted most quickly with the quadrant scales, but they can also be set easily by direct measurement. If a bevelled millimeter scale, or ruled glass plate, is laid upon a grating, its zero corresponding with a white zero thread, when the scale is set at 40° it will be seen that a dimension bounded by two white threads corresponds to the standard. It is easy to increase or diminish it by one or more millimeters by moving the sway-bars. The longitudinal and transverse dimensions are gauged therefore by a reticulated horizontal screen, and the vertical dimension is measured by a vertical screen something like a lawn-tennis net (Pl. XXVIII, 16). It is a single or gridiron grating and has three white threads, the lower of which corresponds to the basal zero plane and the upper to the vertical dimensions in the standard cat and rhesus. It is provided with a graduated quadrant (Pl. XXVII, 33) and can be adjusted and fixed by means of this, or by direct measurement, in the manner described.

In practice, when the several dimensions of a selected head have been ascertained with the needle gauge, the divisions of the gratings, which correspond to the number of millimeters in the corresponding dimensions of the standard, are made to measure the same as they do in the selected head, either by the quadrant scales or direct measurement. In the former case, the grating representing the dimension is set at millimeters by bringing the index of its quadrant scale to 40°; the dimension of the selected head must measure the same as the standard, or more, or less. If the same, the scale being at 40° is correct, if more, or less, the needle gauge gives the amount of the variation in millimeters. The equivalent of the millimeters in degrees of the quadrant scale can be stated as a simple proportion sum, as already explained, and this can be read off on a mechanical calculator if desired. The number of degrees, so determined, must be added to or deducted from 40°, at which the index has been set, and which is reckoned as zero on the quadrant scale. The method of applying direct measurement has been explained.

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Having set the gratings, the next step is to define the index point with the two needles referred to.

The **index point** is the representation, in the indicator, of the objective point in the brain; it is identified in a chart and its distance from the three zero planes determined; the same distance is measured in the gratings, by counting the divisions from the zero lines. In the reticulated horizontal screen, it is identified as a mesh, the required distance from the zero lines representing the interaural and median sagittal lines, and in the vertical screen, the given number of horizontal divisions above or below the white thread representing the basal zero. The actual position of the index point is defined by two index needles. A horizontal radius bar (Pl. XXVII, 23) is fitted in a rotatory joint (20) from which it can be projected by rack and pinion (22), the joint is pivoted (20) on the plate (1) which carries the gratings, outside them, so as not to interfere with their movement; by rotation on the pivot and projection from the joint, the distal end of the radius bar can be made to travel all over the horizontal screen, which it nearly touches, by a series of concentric curves and so brought to any mesh of the screen. At the end of the bar there is a V-shaped slot carrying a vertical index needle (24) which can be raised or lowered and fixed with a screw (25). This needle can therefore be made to coincide exactly with the measured mesh of the screen and represents the position of the index point in two dimensions, it is the required distance from the interaural and median sagittal zero lines. By a similar arrangement, the position of the index point in the vertical dimension is defined by a horizontal index needle (Pl. XXVIII, 29). A vertical radius bar (27), like the one described, is moved by rack and pinion in a rotatory joint (30) pivoted above the vertical screen (16). The bar can be moved all over the vertical screen, with which it is almost in contact, and brought to any of its horizontal divisions; a slot (28) at the end of the bar (27) carries a horizontal index needle (29) which can be projected in its axis and fixed with a screw. By the rotation and projection of the radius bar, the horizontal index needle is brought to any point in any required horizontal division of the vertical grating and adjusted so that its point reaches the vertical index needle at this level; the vertical index needle can be raised or lowered till their points meet and this is the position of the index point (Pl. XXVIII) determined by the corrected gratings in three dimensions. The definition of the index point by

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bringing the points of the vertical and horizontal index needles into contact, as described, is the simplest in principle, but in practice such adjustment of the points of two needles, at right-angles to one another, requires some manipulation. The following plan is more convenient: The vertical index needle (Pl. XXVIII, 24) is replaced by a small square rod, which can be raised and lowered in the V-slot at the end of the radius bar (23), but is not liable to rotate; a short horizontal arm, projecting from this rod, terminates in a minute horizontal cross and the index point projects upwards for half a millimeter from the point of intersection of the arms of the cross. When the horizontal index needle is in contact with the upper surface of any of the arms, the index point reaches to half the thickness of this needle. The cross is brought over a given mesh in the horizontal screen; the horizontal index needle, adjusted to the correct height by the vertical screen, is brought over the cross, which is raised till an arm touches the horizontal needle, when it is fixed. The apex of the index point is then level with the center of the horizontal needle and, at the same time, directly over the given mesh, and therefore the required distance from the three zero planes; the operating needle is directed to this point.

In the three-dimensioned indicator represented in the illustrations, the horizontal radius bar is very close to the horizontal grating and the vertical movement of the cross, with the corresponding excursion of the rod which carries it in the slot of the radius bar, involves pushing the lower end of the rod through the meshes of the horizontal grating, which tends to slacken the threads. To obviate this it is better to have two crosses, one above the other, either of which can be selected, and if the upper or under surfaces of the crosses are alike, either will serve to represent the index point; as the rod can be reversed, the operator has the choice of eight index points at different levels to select from and one of them can be brought to the required height with very little adjustment. A sketch of this device is given in Plate XXVIII. A.

A square rod (1) fits the slot in the horizontal radius bar (23) and can be raised or lowered and fixed with a screw; it has two horizontal arms (2 and 3) one above the other in the same vertical line; each of them bifurcates and terminates in two small rings which hold the central pivot of the cross between them allowing it to rotate in the horizontal plane. The cross is a miniature wheel with four spokes,

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the nave is a little tube, about 2 mm. in diameter and 3 mm. long; the two ends are the same distance from the spokes and either of them serves for the index point (4, 4′, 5′.) Being in the same vertical line, a needle (8) can be passed through both to the marked mesh of the horizontal grating, which it can penetrate without interfering materially with the threads, and ensures the correct position of all the index points in two dimensions, longitudinal and transverse. The arms of the cross, corresponding with the longitudinal and transverse threads of the grating, help to bring the needle (8) directly over the marked mesh. If neither of the horizontal arms (2, 3) is near enough to the level of the index point on the vertical grating, the rod (1) can be reversed and the lower ends of the tubes or naves of the wheels 4′, 5′ will be uppermost and one of them can be taken for the index point. It must be raised by elevating the rod (1) till an arm of the cross is in contact with the under surface of the horizontal index needle (29) which has been brought directly over it. The index point, *i. e.*, the upper end of the tube, will then be level with the center of the horizontal index needle, and the operating needle can be directed to this point as previously described.

The **vertical grating** is attached to the plate of the indicator with two screws (17) and is removed as soon as the index point has been defined, to allow free play to the operating needle, which can be used with either cage or equatorial. The only difference between this indicator and that with a ruled card previously described is in the method of defining the index point by adjustable gratings and making the necessary correction for variations in size once for all. The application of the cage, or equatorial carrying the operating needle, is identical in both forms. This has been described and the advantages of employing single or duplicate instruments have been explained.

Two-Dimensioned Indicator.—The first indicator constructed was the two-dimensioned pattern illustrated in Plates XXV, XXVI. It was designed and employed for directing the inclination of the needle in one plane in the rectilinear machine. As the three-dimensioned pattern just described serves the same purpose, it is not necessary to procure both instruments, but the latter is more expensive and the question may occur to anyone who proposes to work with the rectilinear machine whether the two-dimensioned form, which is cheaper, would not suffice for his requirements. No doubt it might, but there is more than one alternative; both forms of indicator can be made

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with adjustable gratings which, when once set, obviate any further corrections for size, or with ruled cards, which are a good deal cheaper, but with which corrections for size must be made by calculation, or with tables. This is objectionable, but it is rather a question of individual taste and opinion and it is therefore advisable to give a description of the two-dimensioned instrument to help the reader to judge for himself. The principle of the two-dimensioned indicator has been explained in Chapter III, and it is only necessary to recapitulate the essential points very briefly. In the rectilinear machine, when the operating needle has been brought, by one movement of the stage, to the edge of a lamella which contains the objective point and is in the same plane as the inclination of the needle, the lamella may be compared to the page of a book, the objective point to a letter on that page and the needle is at the edge of the page with its axis parallel to it. The needle can be fixed at any angle within a limit of 25° and it can be directed to the objective or letter by sight, by the two movements which are available, namely, (1) the second movement of the stage, parallel to the page or lamella, and (2) the projection of the needle in its axis. Of course, it cannot be so directed if the objective is not visible, when, for instance, it is a point in a lamella which is only a hypothetical slice of the cranium fixed in the machine. But, if we remove the head and substitute a scale photograph of the lamella, or a card ruled with square millimeters and with crossed lines representing the zero lines of the chart, and fix this in the machine, in the position of the lamella, so that their zero lines would coincide, we can then direct the needle, by the movements defined, to any point or marked square of given distance from the zero lines, note the position of the needle on its scales, retract it, then replace the head in the machine, trephine and rack the needle to the figures noted on its scales, when it will have reached the corresponding point in the lamella in the brain. To avoid the removal of the head, we may fix the card in a duplicate instrument, direct the needle by sight in the same way and copy the movements by corresponding scales in the operating machine. Finally, since all those movements are in one plane in the operating machine, they can be accurately reproduced if the card is fixed in a square frame; one side represents one of the guides of the stage and carries a slide block to which is pivoted an extensible needle, or finder, with a quadrant and scale, by which the finder can be set at a given angle. By the movement of the slide block on the guide,

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and the projection of the finder in its sheath, which correspond to the two available movements in the operating machine, the finder is directed, by sight, to the marked square. The dimensions of all these structures are the same as their counterparts in the machine and they have identical scales; it is, therefore, easy to copy them and bring the operating needle to a point, at the same distance from the zero lines of the lamella as the marked square is from the crossed lines of the card. In the operating mechanism of the rectilinear machine by applying the stage to different surfaces of the cage, by a single movement, the needle can be brought to the edge of a frontal, sagittal, or horizontal lamella. In lamellæ of different planes the crossed lines represent different zero lines. By varying the position, or point of view, the card in the indicator can be made to represent lamellæ in different planes, the crossed lines representing different zero planes accordingly. The adjustment required to make the indicator correspond with the operating instrument in different planes will be soon recognized and is facilitated by assuming a section of the machine in the plane of the lamella; the correspondence of the counterparts in the indicator and the plane section of the machine will then be obvious. This is the two-dimensioned indicator in its simplest and cheapest form. It fulfils all the requirements for heads of standard size, but in practice these are rarely found and the square millimeters of the card must be corrected for variations of size in the corresponding dimensions of the selected head, by calculation or by substituting an adjustable reticulated screen for the card. The arrangement of such a screen has been sufficiently explained and is shown in Plate XXV; the frame carrying the needle is applied over it (Pl. XXVI).

The details of the instrument illustrated in the plates require some further explanation. In the **gratings** shown in the plates of the three-dimensioned indicator (Pl. XXVII), which would also be used for the two-dimensioned form in future, the divisions are approximately millimeters. They can be set to measure millimeters, or more, or less, but it was difficult to get gratings made as small as this at first, so it was necessary to double the size of everything in the indicator, every nominal millimeter measuring two. All parts were enlarged in the same proportion and therefore this did not affect the result any more than reading the scale of the indicator through a magnifying glass, but it made the instruments cumbersome. This

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was obviated in another way. The crossed lines divide every lamella into four quadrants and the objective point must be in one of them. It is, therefore, sufficient if that quadrant only which contains the objective is represented. This plan was adopted; the quadrant is bounded by two zero lines and the index point is defined by counting the required number of divisions of the grating, or coordinates, from those lines. It is necessary that the indicator should be capable of representing any quadrant in a lamella, in any of the three planes. This is provided for by using three movable bars, called zero bars, two of which can be made to coincide with two threads of the corrected gratings and form the sides of any quadrant that is required; the index point being identified by counting the divisions from these zero bars, two of which represent the zero lines bounding any quadrant, in any lamella. It has been mentioned that in the cage, as now constructed, all the diameters from any surface to the zero plane parallel to it are equal; hence the distance from the pivot of the needle to the zero plane perpendicular to it is a constant, measuring 70 millimeters in the machine. In the indicator, the zero bar perpendicular to the finder is, therefore, a constant and is fixed at 70 millimeters from the pivot, or in this particular instrument at double that distance, *i. e.*, 140 millimeters; it is always one of the two zero bars forming the quadrant and is called the first zero bar (Pl. XXVI, 12). When first constructed, the diameters of the cage in longitudinal, vertical, and transverse dimensions were different and the first zero bar had to be varied in accordance with the dimension represented, the letters *L. T. V.* for longitudinal, transverse and vertical were for this purpose, but are no longer required. The first zero bar is brought to coincide with a thread of the grating by sliding the whole frame on plates shown in the illustration (Pl. XXVI, 9) the distance from the finder (28), which moves with the frame, to the zero bar being therefore maintained. The required quadrant is completed by using one of the other two zero bars (13, 14), the one selected depending on the position of the quadrant to be represented; only one bar is required and, therefore, whichever is selected, it is called the second zero bar; as they cannot be distinguished as right and left, for these positions may be reversed, they are identified as second zero bars *A* and *B*. One of these bars is made to coincide with a thread at right-angles to the first zero bar and the quadrant is complete. The bars must coincide with threads, because the index point is identi-

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fied by counting the number of divisions of the grating from these bars. The second zero bars carry scales (25, 26) which move with them and are read by separate indices (27) fixed to the slide block (23) which carries the finder (28). The movement of the finder on its guide (24) is registered by this index and scale and shows the distance of the finder from the zero bar and therefore from the zero line it represents. The finder can be extended in a sheath, and a scale and index (21) show the length projected from pivot to point.

In using this indicator the procedure is as follows: The indicator having been placed in a position to represent the quadrant in which the objective point is localized (as previously mentioned, this is facilitated by assuming a section of the machine in the plane of the selected lamella and comparing the section with the indicator), the next thing is to set the gratings to correspond with the measurement of the two dimensions of the selected head. The first zero bar (12) is then made to coincide with a thread of the grating, it does not matter which, and fixed. It will be seen whether second zero bar *A* or *B* is required to complete the quadrant, this, of course, depending on the quadrant to be represented; whichever is chosen, it is made to coincide with a thread at right-angles to the first zero bar and the quadrant is completed. The index point is defined by counting the number of divisions of the gratings from the two zero bars; the mesh so identified should be marked with a pin or a small roll of paper. The finder (28) is now set at the required angle by its quadrant scale (15) and fixed, then the point (22) of the finder is brought to the marked mesh of the screen by two movements (1) of the slide block on its guide, corresponding to a movement of the stage in the machine, and (2) the projection of the finder in its sheath. The inclination of the finder, shown on its quadrant scale, has been determined; the index on the slide block reads the scale of the second zero bar and records the distance of the finder from the bar and therefore from the zero plane it represents, while a scale and index on the finder and its sheath show the distance from the point of the former to the pivot, by which it is attached to the slide block. The operating needle in the machine is set at the same angle; it is moved the same distance from the zero point on the guide of the stage parallel to one dimension of the lamella, which corresponds to the guide on which the slide block travels in the indicator; and finally, the needle is projected from its sheath till the point is the same number of

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millimeters from the pivot as in the finder, when it will have arrived at the objective point in the brain.

In future, a two-dimensioned indicator on these principles will not be constructed on exactly the lines described and shown in the plates. The difficulty of making gratings with millimeter divisions has now been surmounted; hence, a reticular screen, formed of two such gratings, will be employed to represent the whole lamella instead of one quadrant; the crossed lines will be represented by the white threads extending between the pivots of opposed pairs of sway bars. The indicator, therefore, will be like the first one described with a ruled card, the only difference between the screen and the ruled card being that one is adjustable and the other is not; there will be no zero bars, the frame will not require to slide and the movement of the slide block will be recorded by a scale on the guide, exactly as it is in the stage of the machine. This will be a simpler instrument than the one described and illustrated and it may seem superfluous to have devoted so much space to an indicator which will be superseded. But I think it is desirable, if possible, to describe instruments which have been tried and point out their defects and suggested improvements, rather than to furnish accounts or drawings of designs which have not been tested; for however satisfactory these may appear, it is impossible to be certain that they are so, till they have been tried.

The Equatorial (Pls. XXIX, XXX)

The equatorial is a mechanism for carrying and directing the operating needle. In construction it is similar in principle to the astronomical instrument and, within the available limits, it affords universal movement to the needle and can be substituted for the cage and stage of the rectilinear machine. It is supported on four feet with bolts precisely similar to those of the cage and which fit the slots of either the head-vice or indicator, and the needle, in any position, has the same relation to the three zero planes, and to points at the same distance from them, in both instruments. Therefore, if the needle is brought to the index point in the indicator and the equatorial, after fixing all movable parts, is transferred to the head-vice, the needle will be at the objective point in the head; or, if duplicate equatorials with corresponding scales are employed and the needle is directed by sight to any point of measured distance from the zero planes in the indica-

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tor, by making identical movements, guided by the scales in the duplicate instrument, the needle will reach the corresponding point in the head though the point is not visible. As already explained, the first method has the advantage of simplicity; the second, of enabling the operator to perform operations of some complexity.

The instrument consists essentially of a turntable formed by two flat, concentric, horizontal rings; the outer (Pl. XXIX, 36) fitting and rotating freely round the inner (35) and surrounding the head at the level of the basal zero plane. The inner ring has four bolts (37, 38) on its under surface which fit into the slots of either the indicator or the head-vice and can be locked. The rings are graduated and all movements of every part of the instrument are checked by scales and fixed by clamping screws; but, except for verifying the position and making sure that it has not altered, the scales are not required unless duplicate instruments are employed. If it is intended to work with a single instrument, all the scales, except that which registers the projection of the needle, can be dispensed with. An arch (40), like the declination circle, passes across the outer ring to which it is perpendicular and to which it is attached by two terminal feet (42) which slide on rectilinear guides (41) fixed to the outer ring. The whole arch, therefore, has a rectilinear sliding movement, at right-angles to its own direction, by which it can be carried completely across the rings, and the head within them, in any position. A slide block (44) to carry the needle (98) is fitted to the arch and travels completely across it and can be fixed at any point with a clamping screw (45). The outer sheath (72) of the needle-holder is attached to the slide block by a quadrant (47), without which the projection movements of the needle in its sheaths would all be radial from the periphery of the arch towards its center. With the quadrant, which permits free inclination of the needle on both sides, its projection can be made rectilinear and parallel to any horizontal or vertical plane. The same needle-holder and needles are used as in the rectilinear instrument and have been fully described (Chapter IV). The excursion of both sliding and racked movement is registered by the same adjustable index attached to the outer sheath and a millimeter scale engraved on the left of the bed. There are thus five separate movements of the needle available, all of which are registered by millimeter scales and can be fixed at any point by screws. These movements are:

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Movements.—1. Rotation of the outer round the inner ring; this rotation is complete and in either direction.

2. A rectilinear sliding movement of the arch on guides fixed to the outer ring, available in any position of the ring.

3. A movement of the carrier over the whole extent of the arch.

4. Inclination of the outer sheath of the needle on the carrier, regulated and measured by a quadrant.

5. Projection of the needle: (1) By sliding the inner in the outer sheath, and (2) by racking the bed in the inner sheath. Both movements are read by the same scale and index.

As the movements are independent and all of them can be employed separately or together in any combination, the needle can be moved from any position in any direction to any point.

Quadrant Scales (Pl. XXVI)

Adjustment of Grating.—The gratings of the indicator can be easily adjusted by direct measurement with a bevelled-edged millimeter scale or a ruled glass plate laid upon the threads. The zero on the scale is made to coincide with the zero thread of the grating and then the sway-bars are moved till the given number of divisions measure the required number of millimeters.

Graduation of Quadrant Scales.—The gratings are also provided with graduated quadrant scales by which they can be set more quickly. There are a few points in the use of these scales which require explanation. It would appear at first sight that the degrees of the quadrant scale should be equivalent to millimeters in the grating; for example, if the threads of the grating are 1 mm. apart, and a dimension, which is 30 mm. in the standard, is found to be 33 mm. in the selected head, we must add 3 mm. to the dimension, as it is represented in the grating, and make 30 divisions measure 33 mm. Apparently this ought to be effected by moving the sway-bars 3° on the quadrant scale, but this is not possible, for reasons which will be evident.

Inclination of the sway-bars affects all the spaces between the threads equally and, therefore, varies a dimension of 30 divisions twice as much as one of 15; hence, the value of a quadrant degree, for increasing or diminishing a given dimension, depends upon the number of its divisions. Now the gauge is graduated and the difference between corresponding dimensions of different heads is expressed in millimeters irrespective of the number of their divisions, and the millimeter

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is a constant unit, independent of the size of the dimension, whereas the quadrant degree is proportional to it. To find the number of degrees equivalent to the millimeters, which represent the difference between the dimensions, we must multiply the millimeters by a number proportional to the number of divisions of the dimension, and the result may be called the coefficient for that dimension.

A convenient unit to select for a degree of the quadrant is one which varies every interval in the grating 1/40 of a millimeter. If the threads were in mathematical contact at zero on the quadrant scale and the sway bars were moved to 40° the threads would be 40/40 of a millimeter, *i. e.*, 1 mm. apart, and as millimeters are the units of the standard cranium, 40° is made the actual zero of the scale; in other words, when the quadrant scale is set at 40° the divisions of the grating represent millimeters. If we have to deal with a dimension which measures 40 mm. in the standard, for example, the vertical diameter in the rhesus, and set the quadrant of the vertical grating at 40°, the 40 spaces representing the dimension measure 40 mm. If the corresponding dimension in the selected head measures 41 mm., and we move the sway-bars to 41° on the quadrant, we add 1/40 of a millimeter to each division, *i. e.*, 1 mm. to the whole dimension, which now measures 41 mm. as it does in the selected head. But if our dimension had been 20 mm. in the standard, represented by 20 divisions of the grating with the scale at 40°, and the corresponding dimension measured 21 mm. in the selected head, then, if we moved the sway-bar to 41° on the quadrant, we should add 20/40 of a millimeter to the 20 threads and increase the whole dimension half a millimeter. So, to get the required increase of 1 mm. we must move the sway-bar 2° or, as we may express it, for a dimension of 40 mm. the coefficient is 1, for one of 20 mm. 2, for 30, 4/3, etc. A table of coefficients for any probable dimensions of the cranium of the cat and rhesus is appended, calculated to one place of decimals, which is sufficient for practical purposes. It is only necessary, with a given dimension, to find the difference between the standard and selected heads in millimeters, multiply this number by the coefficient for that dimension and the result is the number of degrees on the quadrant which must be added to or deducted from 40, as the selected head is greater or less than the standard. It may appear from this description that it would be quicker and simpler to measure the grating than to make the calculation required to set the scale; in practice it is not so, the

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difference between corresponding dimensions is rarely more than 2 or 3 mm. and, with a table of coefficients, the correction is made at sight; even without the table the calculation is a very simple one. Since at 40° the divisions of the grating represent millimeters, for a given dimension a millimeter has the same proportion to a degree on the scale, as the number of divisions in the dimension has to 40. Stated as a proportion sum, the number of divisions in a dimension: 40:: number of mm.: number of degrees on the scale. If desired, this can be read off on the mechanical calculator (Chapter VII, Pl. XXXVI). If 40, which represents millimeters on one of the scales of the calculator, is made to coincide with the number of divisions on the other, any number representing millimeters on the same scale as 40 will coincide with a number that represents degrees of the quadrant on the other scale. A table of dimensions of the cranium of the cat and rhesus monkey with their coefficients is given here.

Dimension	Coefficient
16 mm.	2.5
18 mm.	2.2
20 mm.	2.0
22 mm.	1.8
24 mm.	1.6
26 mm.	1.5
28 mm.	1.4
30 mm.	1.3
32 mm.	1.2
34 mm. } 36 mm.	1.1
38 mm. } 40 mm.	1.1
42 mm. } 44 mm.	.9
46 mm. } 48 mm. } 50 mm.	.8
52 mm. } 54 mm. } 56 mm.	.7

Rule for Setting Gratings by Quadrant Scale.— Set the scale at 40°. In the given dimension find the difference between the standard and selected heads in millimeters. Multiply the number of millimeters by the coefficient for that dimension; the result is the number of degrees which must be added to 40, or deducted from it, as the dimension of the selected head is greater or less than the standard.

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CHAPTER VII

ILLUSTRATED DESCRIPTIONS OF INSTRUMENTS (CONCLUDED)

Mechanical Calculator (Pl. XXXVI); Stereotaxic Instrument for Spinal Cord (Pls. XXXVII, XXXVIII, XXXIX); Operative Procedure

Mechanical Calculator (Pl. XXXVI)

The simplest and cheapest form of stereotaxic instrument that can be made is probably a rectilinear machine constructed on the same lines as that described here, engraved with millimeter scales which are employed for the measurement of all movements. These scales require correction for size, possibly in three dimensions, and it is irksome and unsatisfactory to make repeated calculations, however simple, in the course of an operation, especially when a large number of observations are recorded, as in stimulation experiments. In order to avoid this, the extensible scales of different forms, already described, have been introduced. Another method is to use millimeter scales and correct them with a mechanical calculator; this will not prove so convenient as the adjustable gratings, but it is inexpensive and, where economy is of importance, its advantages and drawbacks are worth consideration. There are several forms of such calculators; the slide rule is the most familiar and perhaps the most complete, but it cannot be set quickly nor read conveniently while operating. A much better one for our purpose is the quadrant calculator (Pl. XXXVII). It was shown me by Mr. Vellacott and can be made, if desired, by anyone, with a sheet of cardboard; it can be set much more rapidly than a slide rule and placed where the operator can read it, without moving or interfering with his work. It consists of two scales; One, made of celluloid or cardboard, of quadrant form (1), is ruled, parallel to the vertical side of the quadrant, with equidistant lines dividing it into 100°. As the gratings of the indicator are set by quadrant scales, to avoid any confusion it will be convenient to call this scale the table or constant scale. The other scale is formed by a sector (2), pivoted to the corner of the quadrant and graduated with somewhat larger divi-

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sions. In the pattern shown here, the divisions, compared with those of the table, are in the proportion of 5: 4, but this is not essential and for our purpose the divisions might be the same in both scales. By inclining the sector, its highest number—80 in this case—can be made to coincide with any degree on the table from 1 to 100, and any lower number on the sector can be made to coincide with any degree on the table below that with which it coincides when it is horizontal, *i. e.*, at its full length. The sector, therefore, is an elastic scale, measuring 100° of the table when extended (horizontal), but shortened by inclination, if desired, till it measures only 1°; but whether it reaches 1° or 100°, it divides that distance into 80 equal parts. Of course, this also applies to any number on the sector below 80 and since the divisions, though different in the two scales, are uniform in both and those on the sector are all affected equally by any inclination, the proportion of numbers which coincide throughout the scales is always constant. Thus, if 80 on the sector coincides with 60 on the table, 40 coincides with 30, 20 with 15, 10 with 7.5, etc.

It will be evident that, within the limits of the scales, the solution of any proportion sum, or vulgar fraction, can be read off at sight. For as any number on the sector is to the number with which it coincides on the table, so is any other number on the sector to the number with which it coincides.

As regards fractions, suppose we want 37/79 of 83. Find 83, the whole number, on the table and make the denominator 79 on the sector coincide with it. Every division of the sector is now 1/79 of 83, the number 37 on the sector represents 37 of these parts and it coincides with 38.8 on the table, which is the answer.

Put in the form of a rule, it may be stated as follows:

Find the whole number on the table and the numerator and denominator of the fraction on the sector. Make the denominator coincide with the whole number on the table, then the number the numerator coincides with is the required fraction.

The application of this device to such purposes as correcting the millimeter scales of the instrument for heads of different sizes, or finding the number of degrees on the quadrant scales of the indicator, equivalent to millimeters, representing the difference between corresponding dimensions in various heads, will be recognized in the following examples:

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An operator is using the rectilinear instrument with millimeter scales. He finds that in the selected animal, a rhesus monkey, the prefrontal longitudinal measurement is 53 mm.; in the standard it is 50 mm. He finds, by the chart, that the point to which he wants to direct the needle is 23 mm. in front of the interaural line in the standard. How many millimeters does that represent in this animal? Obviously, the number has the same ratio to 23 as 53 in his animal has to 50 in the standard. If he makes 50 on the sector coincide with 53 on the table, 23 coincides with 24.3 and he racks the needle on the longitudinal scale to 24.3 mm. In a stimulation experiment it may be necessary to measure a number of points in the longitudinal dimension. The sector having been set at 50—53, the correction of any further numbers in that dimension can be read off without altering the calculator.

For setting the gratings of the indicator, it has been explained (Chapter VI) that this can be done quite quickly by direct measurement, and still more conveniently by using quadrant scales, in which case, as the difference between two corresponding dimensions is expressed in millimeters, these are converted into degrees of the quadrant scale by multiplying them by the coefficient for the dimension. A table of such coefficients is given. In the absence of such a table the calculation is a very simple one, but it may save trouble to use the calculator. It is applied as follows:

It has been explained that each dimension of the cranium of either monkey or cat always has the same number of divisions, whether millimeters or coordinates. They are represented, therefore, in a grating, by a constant number of divisions, which are millimeters in the standard animal and may be more or less in others. Adjustment of 1° of the quadrant scale varies every division of the grating 1/40 mm. So, a dimension represented by 40 divisions will be varied 1 mm.; one of 20 divisions, .5 mm. and one of 10, .25 mm. In other words, with a dimension of 40 divisions, 1° of the quadrant is equivalent to 1 mm., and if the dimension has more or less than 40 divisions, a degree will be equivalent to more or less than 1 mm., in the ratio of the number of divisions to 40. Suppose that we want to know how many degrees of the quadrant will alter a given dimension a given number of millimeters. Stated as a proportion sum. As the number of divisions of a given dimension: 40:: the number of millimeters: the number of degrees. The figures are usually so small that to state

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the question in that form is to answer it, but, if preferred, it can be read off on the calculator. Find the number of divisions of the given dimension on the sector and bring it to 40 on the table, then the number of millimeters on the sector will coincide with the number of degrees on the table. Of course, if it is more convenient to make the number of divisions of the dimension on the table coincide with 40 on the sector, the number of millimeters on the table will coincide with the equivalent degrees on the sector. A very little practice with the calculator makes the use of it for such purposes perfectly simple. The equivalent number of degrees must be added to or deducted from 40, and the quadrant scale set at the resulting figure.

A cheap and simple form of indicator has been described (Chapter VI), in which a card ruled with square millimeters is substituted for the adjustable gratings. It has the disadvantage of all fixed scales that it has no provision for corrections for size, which must be made by calculations or other means; the calculator serves this purpose, applied as described for correcting the millimeter scales engraved on the rectilinear instrument.

The calculations required to make the corrections which have been discussed are so simple that the reader may consider there is no need for any of the devices suggested; nevertheless, in practice, he may come to a different conclusion; it is not the trouble of making trifling calculations, which is little enough, but it distracts attention from important matters. In an excitation experiment on the brain a stimulus may give rise to a complex of muscular contractions, which may occur simultaneously in various parts of the body and only last a moment. It may be impossible for one observer to follow them all, but practice, by concentrating his attention, and the knowledge of what to look for, enable the trained observer to recognize a good many simultaneous movements. He must analyze, formulate and record them quickly and everything must wait till he has entered them in his notes. It is easy to record details like the time from a clock, or the date from a calendar, more or less mechanically, but even a simple calculation distracts attention and breaks the train of thought. Automatic correction is the best, calculation the most objectionable. A mechanical calculator is a compromise which, without securing all the advantages of the first, avoids some defects of the second.

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Stereotaxic Instrument for Spinal Cord (Pls. XXXVII, XXXVIII, XXXIX)

A stereotaxic instrument for introducing insulated needles for electrolysis, or stimulation of small areas or tracts in the spinal cord.

These plates illustrate an instrument for applying the principles, which have been explained, to the spinal cord, on lines which are essentially similar to those adopted for the brain. The instrument consists of a cradle (1), with four legs terminating in rather blunt points which are curved inwards. The legs are moved on pivots toward the middle line by levers (2, 3, 4, 5) fixed with rack and pinion. By these four grips, the cradle can be quickly and firmly attached to the vertebræ. The cradle supports a travelling stage (10), parallel to the surface of the cord, which carries a needle-holder, and there are two graduated movements in the plane of the stage and one perpendicular to it, by which the needle is directed to any required point. The topographical method employed is also somewhat similar to that described for the brain. The objective point is localized in a transverse section of the cord, perpendicular to the stage and parallel to the needle, or in a chart of the section photographed to scale. This transverse section may be regarded as a lamella and the needle is brought opposite to the edge of it by the longitudinal movement of the stage parallel to the spine. The needle is then directed to the objective by two movements: (a) The transverse movement of the stage and (b) the extension of the needle in its sheath (23). The objective point is identified by millimeter measurement from two zero lines, one of which corresponds to the longitudinal division of the cord, connecting the anterior and posterior median fissures. Assuming the prone position of the animal, the spine horizontal with its dorsal aspect uppermost, this is called the vertical line, the other perpendicular to this, like the crossed line of the letter T, rests on the surface of the posterior columns. The lateral distance of the needle from the first or vertical line is measured by the horizontal scale and adjustable index on the back of the sheath, which records the lateral movement of the needle from a zero, set to correspond to the posterior median fissure.

Balance Gauge.—The depth or distance of the needle from the second or horizontal line is given by a scale (19) and adjustable index on the bed (14) which record the extension of the needle from a zero, set to correspond with the surface of the posterior columns, when the stop and point of the needle are just in contact with them.

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It is evident that the vertical or extension movement of the needle must be parallel to the first or vertical zero line, and as we cannot depend on fixing the cradle so accurately as to secure this, it is provided for by the balance gauge (9) which fits the sheath (23) of the needle-holder. This consists of two vertical parallel rods carried on a brass plate, from the front of which project two small transverse shelves, both perforated with holes for the two rods, which move freely in them in a direction perpendicular to the stage and the surface of the posterior columns. The lower extremities of the rods, 2 or 3 mm. apart, rest on the posterior columns of the cord; their upper extremities terminate in small cross-plates; and when these two cross-plates are level, the rods are perpendicular to a line connecting their lower ends, which are resting on the posterior columns; *i. e.*, the second, or horizontal, zero line. In order that this position may be secured and maintained for any movement, with any needle, the sheath (23) is pivoted and swings on a quadrant (8) and can be fixed at any point by a screw (not seen in the illustration). The front of the plate is ruled with horizontal lines, which show when the T-pieces on the tops of the rods are in line.

Direction of Needles.—In practice, when the carrier has been brought to the required section or lamella, by the longitudinal movement of the stage effected by the screw (12), the balance gauge is introduced and adjusted by the transverse movement till the ends of the rods rest on the posterior columns of the cord. The T-pieces are brought into line by adjustment of the sheath in the quadrant and the latter fixed with the screw. The gauge is now removed and the pilot needle, being introduced, will be perpendicular to the transverse zero line and, of course, parallel to the vertical one. A preliminary puncture of the membranes and cord is made by the pilot needle (11), which is then removed and the insulated needle introduced in its place. The point of the insulated needle is made level with the surface of the stop (21), the needle-holder is pushed down in the sheath till the stop is in contact with the surface of the posterior columns of the cord, and the adjustable index (20) is set at zero on the scale (19) of the bed. The needle is then projected by means of the screw (22) to the correct depth from the horizontal zero line shown by the scale (19) on the bed (18).

Suggested Improvement.—There are one or two defects in this instrument which must be corrected as soon as possible. The principal

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one is that it is necessary to expose the vertebræ for about 5 cm. to fix the cradle by these grips. This involves a fairly large wound, so that, in its present state, the instrument is not applicable to animals which are allowed to survive the anæsthetic and should not be employed for degeneration experiments. But it seems practicable to substitute needle grips for those now employed. They will puncture the skin and hold the cradle sufficiently firmly to the spine, without exposing it beyond the smallest median incision sufficient to give access to the very limited area required.

As the travelling stage, with the electrolytic and other needles, can be fitted to any cradle, the alteration required will be very slight and will not affect the rest of the instrument.

It is probable that for the small but deep wound required to reach the cord, some special retractors or specula may be necessary. To divide the laminæ of one vertebra which should be sufficient, a small trephine or fine bone forceps with long points will be most suitable; and as it is not very easy to define the posterior median fissure without dividing the membranes, which is undesirable, a pair of fine, curved blades will be fitted on to a pair of forceps or calipers attached to the stage. They will be introduced on both sides of the cord and support it with very light contact. The lateral movements of the needle will be directed by a small gauge, extending across the cord from one blade to the other. The details of this procedure have yet to be worked out.

The adaptation of these needle grips for securing the cradle and facilitating the introduction of the electrolytic needle to the spinal cord through a small wound should not present any serious difficulty; but it is an object of real importance, because the infliction of a relatively large incision is at present the only obstacle to a very precise application of the degeneration method to the cord and the development of a promising field of anatomical investigation. In other respects, the requirements of this method are amply provided for; there is no reasonable limit to the fineness of the electrolytic needles and precisely circumscribed, pin-point lesions can be produced anywhere. The restricted field involved and limited range of the needle are very favorable to accuracy. With a little practice, by making a series of from 12 to 20 separate experiments applied to one small area and finally determining the exact locality of the lesions in sections,

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with the microscope, there is no tract too small to be precisely differentiated and its course completely traced.

Operative Procedure

Sterilization of Instrument.—In performng operations with the stereotaxic instrument there are several details, such as the introduction of the ear cones and treatment of the ears, the measurement of the cat's head, order of procedure, etc., which will be new to all or the majority of my readers and must be explained. Some of them have been mentioned in the description of the parts of the instrument with which they are associated, but presented in a rather disjointed form which an intending operator would have to pick out. Hence it may be useful to bring them together in a connected account of the steps of an operation. This account is specially applicable to the cat, but the procedure is generally very similar in other animals; peculiarities, like certain measurements of the head, and introduction of the ear cones, so far as they are exceptional, require special adaptations in the cat. If an aseptic operation is required, the first point is the sterilization of the instruments. The stereotaxic instrument will not bear frequent boiling, nor is this necessary; except at a few points, it is never in contact with the head, though it affords valuable protection to the wound, which is usually so small and requires so little manipulation that it ought never to be contaminated. The whole instrument should be carefully cleaned after use, washed with boiling water, dried with a soft cloth which has been boiled and dried in an oven, and placed in a bath, large enough to cover it, of strong alcohol, in a vessel provided with a well-fitted ground-glass cover. Parts that come in contact with the head, such as the mask, ear cones, guides, grips of the lateral screw clamps, trephines and forceps and also the pilot and other steel needles, should always be very carefully cleaned and boiled before they are put in the spirit bath. The ivory bed of the needle should be removed from the inner sheath; the latter terminates in the stop which may touch the wound; this part can be held in boiling water for a short time before the whole sheath is placed in spirit. The extensible and ivory scales and ivory bed of the needle cannot be kept in alcohol, but they should never come in contact with the head of the animal nor the hands of the operator when they are in position. They may be cleaned with a boiled rag dipped in 10 per cent formaldehyde and then in boiled water. Plati-

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num and glass needles are best sterilized in pure nitric acid and then boiled water.

Preparation of Animal.—Cats which are to be operated on aseptically should always be prepared, if possible, a few days before the operation, their heads shaved and measured and the ears thoroughly cleaned under an anæsthetic. These preparations take longer than the operation; the animal must be fully anæsthetized the whole time, and it is inviting gratuitous disadvantages to add the depression of prolonged anæsthesia to that incurred by the operation itself. If the preliminaries have been carried out previously, the instrument made ready and the extensible scales adjusted, as soon as the animal is anæsthetized the ears can be quickly washed again (or this may be omitted), the skin, where it has been shaved, washed with spirit and painted with tincture of iodine, the ear cones introduced, the instrument applied, and the operation quickly completed. It is impossible to exaggerate the importance of reducing the shock of the operation by every means in our power. This is desirable on various grounds, not the least of them being that compensation so quickly masks the disabilities produced by a small lesion, that rapid recovery, permitting early examination, may afford information of the greatest value which would otherwise be overlooked.

Treatment of the Ears.—The ears need careful treatment and should be attended to some days before an operation. It is impossible to sterilize a cat's meatus efficiently, and as the introduction of the ear cones requires some manipulation, unless care is exercised there is a risk of septic infection. The ears should be thoroughly washed out with hot water and soap applied with a very soft shaving brush. The skin is thin and may be excoriated if a stiff brush is used. After the soap has been washed away, the cavity, especially the deep parts, should be dried with absorbent cotton and then painted with an antiseptic ointment. Equal parts of boric acid and oxide of zinc, mixed to the consistency of thick cream, with olive oil, glycerine and water, with the addition of 1 per cent of lysol, serve the purpose.

Application of Mask.—The mask (Pl. II) is first fitted on. The orbital brackets (9) are made to correspond to the centers of the orbits, over the lower margins of which they are hooked. The bit (8) is inserted in the mouth behind the upper canine teeth. The screws (16) are passed through the slots and secured moderately firmly by the split nuts (11).

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Introduction of Cones in Cats.—The auditory meatus in cats, especially in old ones, where it is deeply sunk between the mastoid process and masseter muscle, is not very accessible. The pinna forms a deep funnel tapering to quite a small apex and the opening of the meatus is not exactly at the point, but joins it rather obliquely, the folds are irregular and the orifice is further concealed by cartilaginous lips, so that it is merely a slit which may be invaginated by the blunt point of the ear cone. Moreover, as the outer part of the meatus is composed of cartilage and loose fibrous tissue, if the cone is not introduced in the axis of the bony canal it may miss it and lodge in the tissues, although it has entered the orifice. The easiest plan is to split the funnel by cutting the anterior inferior aspect of the pinna down to the apex; this exposes the orifice of the meatus and makes it easy to insert the cone; but it is an objectionable proceeding if the animal is to survive, because it leaves an open wound which may bleed freely and is liable to septic infection. The necessity, however, can be avoided with a little trouble. It is sometimes advisable to use a guide like that shown in the illustration (Pl. I, 1). The guide is a small steel bar 3 mm. wide fixed at an angle with the handle and is passed into the meatus with or without the aid of a speculum (Pl. I, 111).

Speculum and Guides.—It is easy to introduce the guide without the speculum, but groping is objectionable on account of sepsis and it is difficult to make sure that the guide is in the meatus unless it penetrates to the fundus, which involves perforating the membrana tympani. This is not of very much consequence, but it is preferable to avoid it, so the best plan is to expose the orifice with the speculum, pass the guide a few millimeters into the canal and, holding it there, withdraw the speculum. Keeping the guide in position, another handle terminating in a round probe is used to introduce the cone; the probe is inserted into the lumen of the cone and projects 2 or 3 mm. beyond its point. There is a slot in the disc which is slipped over the heel of the guide and, when fitted on, the point of the cone hugs the guide, slides easily down it, and must enter the meatus; as it is pushed home the guide is gently withdrawn. The cone is held in the meatus by the probe until the clasp (Pl. III, 20) is applied and it holds the cone securely in its place till the head is in the frame, when it is removed.

The funnel-shaped pinna in its natural position is more or less flattened or telescoped and thrown into folds. To expose the orifice

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of the meatus as much as possible these folds should be straightened by drawing the pinna directly outwards.

The method described with the guide is the most certain way of introducing a cone and it is advisable to have the guide at hand and to know how to use it in case of exceptional difficulty, but it is usually unnecessary. If the pinna is drawn outwards, as advised, and the cone is introduced on the probe, the opening will be found in most cases without difficulty. If it gives any trouble, the best plan is to expose the orifice with the speculum and then pass the probe and cone as the speculum is withdrawn. The apex of the funnel of the auricle is so narrow that there is not often room for both cone and speculum together. The advantage of the guide is that it can be introduced by sight while the speculum is in position and exposing the orifice of the meatus.

Anatomy of Meatus in Cats.—Questions may naturally occur as to the effect of these manipulations on the internal ear and membrana tympani and, to answer them, it is necessary to enter into a brief explanation of the anatomy of the parts in the cat. The direction of the meatus is nearly transverse, but the axes of the two tracts converge to a point slightly in front of the interaural line. The canal terminates in the huge bony air cell, seen in many sections in the atlas, which has been described as the bulla ossea. In shape it is something like a hip-bath, deeper behind than in front, with the edges bent over to form a rounded rim, projecting above the level of the membrane, which is attached to the edge and stretching across the oblique opening extends downwards, forwards and inwards, at an angle of about 45° with the interaural line. The posterior margin of the membrane extends some 8 mm. further out from the median line than its anterior insertion, and at the latter point the cava tympani, the space between the membrane and the inner wall of the bulla, is not more than 2 or 3 mm. deep. Near the posterior attachment of the membrane, where the roof meets the posterior wall of the meatus, the head of the malleus is articulated and its handle, which is exceptionally long, accompanies the membrane almost to its anterior insertion, pointing in the direction of a lower molar tooth on the opposite side. The labyrinth is above and behind the head of the malleus; it is quite out of reach and need not be considered. The cones are not long enough to reach the membrane and if they were it would be difficult for them to perforate it owing to

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its obliquity. If the guide is made to penetrate far enough, it punctures the membrane in the anterior inferior quadrant near the tip of the manubrium and is immediately brought up by the inner wall of the bulla. I dissected one or two specimens where this occurred, to see the effect, and at first could not detect the puncture, but found there was a valvular opening in the situation indicated through which the guide had passed. The membrane is thin and not very vascular, the slight rent could make very little difference to the animal and was obviously of small importance.

A more serious matter is the practical impossibility of sterilizing the meatus and therefore the less manipulation there is in it the better. It is desirable to introduce the guide and cones without groping and a beginner should practise it in some animals which are to be destroyed while still anæsthetized, before attempting it on one which is to be kept alive.

Application of Head Instrument.—The mask having been fitted on and secured moderately firmly with the screws and the cones introduced, the next step is the application of the *head-vice* (Pl. V, VI, VII), which is suspended by four springs and supported on a stand. It is brought directly over the animal and lowered till the head can be easily raised into it. While an assistant steadies the frame, the operator lifts the head from below and slides the conical extremities of the aural pivots (Pl. V, 26) into the orifices of the ear cones, making sure that they are well home. The horizontal arms (14) of the mask are raised till they are in contact with the under surface of the lateral bars of the frame and fixed there with the clamps (Pl. VI, 46) provided for that purpose. These clamps must be fixed at the same distance from the pivots, *i. e.*, the interaural line, the lateral bars (22) of the frame being graduated with this object. It will be seen at this stage that the basal zero plane of the cranium coincides with the upper surface of the head-vice. The occipital bar (Pl. VI, 24) is brought forwards till it is in contact with the occiput and clamped, at the same distance from the interaural line, on both sides. The cranium is then centered with the four screw clamps (Pl. VI, 27-30) and the aural pivots (25), which are all graduated and can be easily read from the same point in front. The screw clamps should be slipped up as far as they will go, followed by the screw nuts (28-31), and a turn or two of the latter will secure a firm grip of the head. They must be adjusted to exactly the same reading on both sides, and

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when the screw clamps and aural pivots read exactly the same on both sides, the sagittal zero plane of the head and the median longitudinal plane of the frame must coincide. All screws must now be fixed and the position of the head in relation to the frame carefully inspected. If this is not true, there must be some error in the application which must be looked for and corrected. The cage (Pl. X) is next dropped into its slots (42, 43) and fixed by the four screws (44, 45), and the cranium is then measured with the needle-gauge (Pl. XXII) from above, from both sides and from behind. The anterior longitudinal dimension of the cranium in the cat cannot be measured directly without opening the frontal sinus, but we may estimate it approximately by the posterior margins of the orbits (Chapter V). One method of measuring the latter is with screw rods (12, 13) attached to the mask, the rods terminating in clefts which engage the margins of the orbits. This method is shown in the illustrations; the posterior margins of the orbits can also be measured directly with a gauge (Pl. XXXIV, 34), which is preferable.

Setting Scales.—Having measured the cranium the figures are compared with those of the standard head. When they are identical, or nearly so, millimeter measurements are employed for that dimension; but if they are greater or less than the standard in any dimension, the extensible scale (Pl. IX), which corresponds to it, is set so that its divisions measure more or less than millimeters in the same proportions. The scales, having been set, are inserted in their clamps in the travelling stage (Pl. XIII, 84, 85) and the needle-holder (Pl. XIV, 112).

Traversing Stage.—The traversing stage (Pl. XIII) is then applied to the cage in the position required for introducing the needle, having regard to the point to be reached, and the direction by which the needle is required to approach it, (Pls. X, XI, XII). The traversing stage is fixed to the cage in any desired position by means of steady pins and two clamps (Pl. X, 90). These must be firmly secured. If the pilot needle is to be used (Pl. XVI, 1), it is next attached and by the two movements of the traversing stage is brought directly over the objective point in the cranium, the stop (97) pushed down a convenient distance and the needle racked through the stop till it reaches the bone, which has been exposed by a small incision through the integuments.

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Pilot Needle.—The point of the pilot needle indicates the center of the trephine hole which is to perforate the skull. This point should be marked with a fine drill set in the rectangular handle of the dental engine. It is made to penetrate a short distance into the bone exactly where the pilot needle touches it. Having marked this spot, the pilot is withdrawn and racked out of the way by the traversing stage, leaving the head exposed sufficiently to allow the application of the trephine. The trephine is fixed to the dental engine and the small disc of bone removed; the hæmorrhage, which may be considerable for the size of the wound, is checked. Then the pilot needle is brought back to the original position and racked down through the dura till it reaches the objective point, which is known by the scale and index of the rectilinear needle (Pl. XIV, 111, 112, 113).

Setting Rectilinear Needle.—When these have been set and the adjustable index (113) on the bed of the needle reads both the ivory and extensible scales at once, they are required to show, at any time, the distance of the point of the needle from the zero plane parallel to the stage in millimeters and in coordinates. To secure this we must: (1) See that the point of the needle is exactly level with the stop (97); (2) slide the latter down, by the movement of the inner in the outer sheath, to the point required close to the dura or touching it, and lock the holder with the milled head (96); (3) read the distance of the stop from the zero plane, with the scale of the stop and arrow on the side of the inner sheath; the point of the needle is the same distance and we must, therefore, (4) set the adjustable index (113) to read the same on the ivory scale (112); (5) see that the spiral, which is to represent zero in the spring scale, corresponds with zero in the ivory scale. Then in any position of the needle point the ivory scale (112) will show how many millimeters it is from the zero plane, the extensible scale (111) how many coordinates or corrected millimeters. We know from the chart how many millimeters or coordinates the objective point is from the zero plane; and whether we use millimeters or coordinates the number is always the same. So we have only to rack the needle down till the index reaches the same number on the scale in use, and the point of the needle will have arrived at the objective. The pilot needle is now withdrawn and for interchanging needles it is advisable to remove the inner sheath by relaxing the milled head (96) and pulling the whole sheath and needle out by it. The pilot with its bed is removed from the

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inner sheath and the electrolytic or other form of needle already mounted on its own bed is substituted for it, the point of this needle must also be made to coincide with the surface of the stop; it is then introduced again into the outer sheath, pushed down till the stop is in the previous position, which must be verified by looking at the scale on the inner sheath, and locked. If the position of the stop is altered the adjustable index must, of course, be altered accordingly, and the operator must never forget to see, when reading the scale on the inner sheath and setting the adjustable index, that the needle and stop coincide and that the zeros of the ivory and extensible scales do the same.

Inclined Needle.—This procedure applies to any rectilinear movement of the needle; if the needle is inclined, the method of measurement is different. The objective point is located in a lamella parallel to the plane of inclination of the needle and perpendicular to the stage, the needle is brought to this lamella by one of the movements of the stage which may be called its first movement and is measured by the extensible scale, if that dimension of the head differs from the standard. There remain the second movement of the stage and the two extension movements of the needle in its sheaths, to bring the point to the objective. The measurement of these movements is ascertained by the indicator and copied in the instrument. They comprise the angle of inclination, length of needle and number of millimeters from zero of the scale which records the second movement of the stage. These readings are always in millimeters, because the correction for size in both dimensions of the lamella is effected by the adjustable grating of the indicator and, therefore, extensible scales are not required. The adjustment and application of the indicator having been fully described elsewhere (Chapter VI), it is enough to say here that the grating of the indicator represents the lamella and is adjusted to correspond with its variations of size; the objective point is located in it by measurement from zero bars which represent the two zero planes and are used for the same purpose. A frame, carrying a finder needle and graduated quadrant, exactly reproduces the needle and its movements in the instrument, with the advantage that it can be directed by sight. The finder needle is set at the required angle with its quadrant, moved on a guide which corresponds to the second movement of the stage and extended by a measured projection from its pivot till it reaches the objective point in the

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grating. The process is exactly repeated in the operating instrument; the needle is set at the same angle by the quadrant, moved the same distance from zero by the second movement of the stage, the first having been employed to bring it to the lamella represented by the grating, finally extended the same distance from its pivot, and the result must be to bring it to the same objective point in the lamella which it has reached in the grating of the indicator. The extension of the needle in the stereotaxic instrument is read by the millimeter scale of the inclined needle on the left of the bed (110) and an adjustable index (Pl. V, 79) attached to the outer sheath. The excursion of the bed in the inner sheath and of the inner in the outer sheath both affect the relation of the scale on the bed to the index on the outer sheath equally, so that the two movements are practically identical and are read indifferently from the same scale and index. This adjustable index is set as follows: The point of the needle is made to coincide with the extremity of the stop, the pivot stop line (marked *P. S.* on the back of the inner sheath) is made level with the top of the outer sheath; this brings the stop and point of the needle level with the center of the pivot, and the adjustable index is then set at zero on the indicator scale (on the left) (Pl. XIV, 110). It will register the distance of the point of the needle from the pivot, whether the former is moved by racking it through the stop or by sliding one sheath in the other. Whichever needle is employed, it is racked through the stop to the objective point, which has already been reached by the pilot. The subsequent manipulation is explained in the separate description of each variety of needle.

Equatorial.—(Pl. XXX.) When the equatorial is employed, the foregoing procedure requires little modification. After the head has been adjusted in the head-vice, the gauging and drilling cage (Pl. XXXIV) is applied and the dimensions of the cranium taken with the needle gauge (26) fitted to that instrument. The gratings (8, 12, 16) of the three-dimensioned indicator (Pls. XXVII, XXVIII), which is always employed with the equatorial, are set in accordance with the measurements of the cranium and the index point is defined by the index needles (Pl. XXVIII) in accordance with the measurements of the objective ascertained by the chart. The index point is fixed in this position and the vertical screen (16) and horizontal index needle (28) are removed, leaving the index point exposed and easily approached from any position by the operating

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needle in the equatorial. The equatorial carrying the pilot needle is then applied to the slots of the indicator and fixed with the clamping screws. The pilot needle is set at any required angle and directed from any selected position and projected till its point is in contact with index point; all clamping screws of the equatorial are now fixed, the length of needle projected to make contact with the index point noted on the scale and the needle then retracted sufficiently to be out of the way. All this can be carried out a day or two before the operation, and it is desirable that this should be done so that the actual operation may be performed as quickly as possible; but in any case when the equatorial has been set in the way described, it is transferred bodily from the indicator to the corresponding slots in the head-vice, fixed, and the pilot needle projected till the point touches the cranium and the point of contact marked with ink or a small drill. The pilot needle can then be retracted again as far as convenient or the whole equatorial removed while the cranium is trephined at the marked point. A 5 mm. trephine is usually sufficient, the crown of bone is removed and any hæmorrhage from the diploe arrested. The equatorial is then replaced, if it has been removed, and securely fixed, the needle is pushed in till the stop is close to the cranium, where it is fixed, and the needle is racked in through dura and brain till the index reaches the number noted on the scale of the needle, when the point of the pilot will be at the objective. The pilot is then withdrawn, another needle substituted, and the required operation completed. If duplicate equatorials are employed, one is applied to the indicator and the other to the head-vice, the steps of the operation are carried out in the indicator and precisely repeated by means of the corresponding scales in the instrument attached to the head.

I hope that as the application of this method becomes known, some medical men with clinical experience who encounter interesting problems in the anatomy, physiology or surgery of the brain, but who have been deterred from attempting to solve them experimentally from want of technical training, may be encouraged to undertake such investigations when they realize how easily, with ordinary surgical knowledge and a little practice, the necessary operations can be performed with the machine. For those who have had no previous experience of operations on animals a few practical suggestions may be useful.

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Anæsthesia.—Compared with the monkey the cat is a bad subject for anæsthesia. It is apt to collapse under chloroform and to get the bronchi choked with excessive secretion under ether. In various laboratories certain routine methods of producing anæsthesia are in favor and, when this is the case, it is generally advisable to follow them. A very satisfactory method is that of sending a current of air from an automatic pump through a Woulfe's bottle containing chloroform alone, or mixed with ether, affording a regular supply of dilute vapor of constant strength. Another plan often adopted is to give a preliminary dose of paraldehyde by the mouth or urethane or morphia by hypodermic injection; full doses produce a heavy sleep in which a very small quantity of chloroform at fairly long intervals is sufficient to maintain prolonged and deep anæsthesia. This is useful when it is necessary to keep the animal anæsthetized for a long time, as in stimulation experiments, but with operations from which the animal is to recover it is not advisable, and inhalation of a mixture of chloroform and ether or A. C. E. as the only anæsthetic is preferable. Great advantages are claimed for various inhalers; most of them give a dilute vapor of fairly constant strength, which is the important thing, and they have arrangements for increasing or diminishing the strength of the vapor at will with more or less accuracy. A cloth folded into a cone or a piece of wool in a wide-mouthed bottle will serve the purpose well enough. Cats should be anæsthetized to begin with under a large bell glass which easily covers them, they will submit to anæsthesia so induced repeatedly without any sign of fear or aversion, but to hold the animal down and begin the administration with an inhaler excites fear and resistance and probably necessitates a larger dose of anæsthetic. Once it is applied the anæsthetic should be administered continuously until the animal is fully narcotized.

Overdose Fallacy.—The belief, which has been sedulously inculcated and widely accepted, that death from chloroform is invariably due to an overdose, in quantity or concentration, is a mischievous fallacy that has probably been responsible for more fatalities than any other error. Dr. Goodman Levy,[8] who has made many valuable observations on this subject and whose work is well known and widely appreciated, has proved that an insufficient dose of chloroform is an effective cause of ventricular fibrillation which is prevented by a more liberal administration. His experiments which are described in numerous papers

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are convincing, but apart from his precise and critical methods a very moderate experience should make two things clear to everyone but those who can see nothing but what they want to: (1) That in many of the cases of death from chloroform the possibility of an overdose can be absolutely excluded; (2) that when it occurs in such circumstances the symptoms are quite distinct from those due to an unquestionable overdose.

In trifling operations in man when the surgeon is content with very light anæsthesia, the administrator is cautious and the narcosis purposely incomplete, the possibility of danger is notorious; and in animals, especially cats, when an anæsthetic is resorted to merely for convenience, to keep the animal quiet in a procedure which could not cause pain, while chloroform is being administered most sparingly and nothing like full anæsthesia has been obtained, the breathing may suddenly stop without warning. Artificial respiration is useless, for when the breathing ceases the heart has already done so and life is extinct. This is quite different from what occurs with an overdose where the subject is fully narcotized; the breathing becomes labored and stertorous before it ceases, the heart generally continues beating and with artificial respiration, inversion, etc., recovery or death may result, but there is generally some response and something like an effort at recovery. In the laboratory, with cats especially, a careful anæsthetist who believes the only danger is from an overdose and has had one or two fatalities, which he is assured were due to that cause though they were really due to his caution, may become over anxious, give a very small dose and frequently remove the inhaler to observe the respiration, keeping the animal fluctuating on the verge of narcosis, which is the very way to produce the result he is so anxious to avoid; whereas a laboratory boy or an inexperienced student will push the anæsthetic freely without any mishap. The safest plan appears to be to get fairly quickly over the borderland of incipient narcosis, to employ a constant vapor containing about 2 per cent chloroform which may be slightly increased till full anæsthesia is established and slightly diminished to maintain it, but applied continuously till full narcosis is established. A practice to be particularly avoided is to get the animal nearly under, then remove the inhaler and let it partially recover.

If it is intended to keep the animal alive after the operation every effort should be made to avoid shock and to secure the most rapid

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recovery possible; it is a mistake to hurry, but it is just as bad to waste time.

Hæmorrhage is generally insignificant and hardly ever severe. Large vessels are not often encountered and still more rarely wounded by the needle in the substance of the brain. They are chiefly met with in the diploe and the membranes. A sinus can be avoided by making a small incision in the dura to one side and drawing it out of the way of the needle with a small retractor. Bleeding from the vessels on the surface of the brain and oozing generally can be checked with peroxide of hydrogen 20 vol. strength applied on a small pledget of wool. It is also sufficient, as a rule, to stop bleeding from the diploe, but if this should be obstinate the galvanic plug (Pl. XXXV) can be used. There is no need of irrigation with hot water and it should be altogether avoided. A cat's fur is very long, fine and close, and when it is saturated with hot water it is hard to say how long it takes to dry. The cat's natural aversion to water is probably due to the difficulty of getting dry. No amount of rubbing with cloths is quite effective. It is not a desirable proceeding just after an operation, and to let the animal spend the night with a wet coat is most objectionable. Operations on the brain, by the method described, produce so little disturbance that cats generally recover from them very rapidly.

After-Treatment.—It is advisable to enter in the notes the time an operation is concluded and the animal returned to its cage, how long it is after when it gets up voluntarily and walks about, when it first takes milk and meat, begins to clean itself, and, of course, its condition the following morning. As a rule, it ought to have got up of its own accord and be sufficiently sensible to come when it is called and take milk, in an hour from the time it is put back in its cage, and the next morning, except for any specific disability which is the necessary and intentional effect of some lesion, it should be perfectly well; feeding well, cleaning itself, its coat and eyes bright and able to run about the laboratory, jump off chairs and tables, etc., as if nothing had happened. Of course, we cannot always secure such good results, but an ordinary operation should not be considered satisfactory unless they are obtained. The accident most difficult to prevent is opening the wound before it has healed. Some cats will constantly rub their heads against the wires of the cage and get a dressing off unless it is very secure. A figure-of-eight bandage of narrow adhesive plaster,

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passed under the jaws and alternately in front of the ears and behind them is the most effective, but care must be taken not to bring it far enough forward to interfere with the movement of the jaws. If it should be necessary to remove it, the hair, to which it adheres, must be snipped with a pair of scissors. I have made some caps which answer fairly well. Two longitudinal wires passing from just above the orbits to the occiput are fastened to two or three transverse bands of leather or poroplastic which extend across the cranium, one in front of the ears, and one or two behind them; they converge to two rings, one on each side, connected under the jaws with a strap and buckle and the cap is attached to a leather collar. It has the advantage of being quickly applied and removed. The best immediate dressing is a single layer of thin gauze, very little larger than the wound, painted with a thick solution of celloidin extending for some distance over the skin. The celloidin dressing should be very thin, for if several layers of gauze are used and these extend much beyond the wound, they may take half an hour to dry, involving a prolongation of anæsthesia which should be avoided.

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PLATES

REFERENCES TO NUMBERS

PLATE I.—EAR CONES, GUIDE, SPECULUM

FIGURE I

Guide for introducing ear cone in cat.

FIGURE II

Probe for introducing ear cone in cat.

FIGURE III

Speculum for introducing ear cone in cat.

FIGURE IV

Method of applying guide and probe to cone.

FIGURE V

A. Plain straight ear cone for cat. The disc is slotted for the gui
shown in Figs. 1, 2 and 4.

B. Another form of ear cone for cat with an adjustable curved flange v
rests against the ramus of the jaw and the masseter muscle.

C. Ear cone for rhesus monkey. The cone is bent at an angle of
20° to correspond with the meatus, the diameter of which is
ject to variation. Two or three sizes of the cone should be
vided; the one represented is about the average. The follo
figures indicate the various parts of the cones illustrated: 1,
2, Angle. 3, Barrel. 4, Disc. 5, Flange. 6, Funnel. 7, Scre
fixing adjustable flange (5, B). As the corresponding parts o
right and left sides of the stereotaxic instrument are identic
reduce the number of figures required, the same number is
to indicate duplicate parts on both sides in the following
trations and each part retains the same number in different p

PLATE II.—THE MASK

Parts previously shown retain the numbers assigned them.

8. Bit, placed in mouth behind upper canine teeth. The figure is p
between the slots which receive the screws (16) by which t
and orbital brackets (9) are made to hold the upper jaw and s
the mask in position.

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9. Orbital brackets which are hooked over the lower margins of the orbits and held firmly against them with the bit (8) and screws (16).
10. Pillars which support screw rods (12).
11. Split nuts with conical points and washers (19) which are applied to screws (16) to raise bit (8) against counter pressure of orbital brackets (9).
12. Screw rods for measuring posterior margins of orbits, the cleft extremities engage the margins of the orbits; when screwed up, the base of the cleft is in firm contact with the margin of the orbit and the stud (15) indicates this point and can be measured from the front of the cage with a depth gauge. The margin of the orbit can be measured directly with a depth gauge fitted with a small transverse bar at its extremity and this method is perhaps more convenient especially with the measuring cage (Pl. XXXIV).
13. Screws for adjusting screw rods (12).
14. Horizontal arms which are held in contact with lower surfaces of lateral bars (22) of head-vice (Pl. VI). When they are in this position the upper surfaces of the lateral bars are level with the lower margins of the orbits.
15. Studs corresponding to the bottoms of the cleft extremities of screw rods (12) and consequently to the posterior margins of the orbits which they serve to measure.
16. Screws which pass through the slots in the bit (8) and with the split nuts (11) hold the bit (8) and brackets (9) together and secure the mask.
17. Front of mask formed by a sliding joint (17) which regulates the distance between the orbital brackets (9). The joint is fixed with a screw (18).
18. Screw for fixing sliding joint (17).
19. Conical washer of split nut (11).

PLATE III.—LATERAL VIEW OF HEAD OF CAT WITH MASK

Lateral view of head of cat with mask and ear cones in position ready to be introduced into the head-vice (Pl. VI). The cones are held with a clamp (20) which is removed when the tapered ends of the aural pivots (26) have been inserted into the cones.

The clefts of the screw rods (12) engage the posterior margins of the orbits, the level of which is marked by a stud (15) on the outer surface of the cleft extremity of the rod.

Figures the same as in Plate II.

20. Clamp to hold ear cones in position till the head is fixed in the head-vice.

PLATE IV.—FRONT VIEW OF SAME HEAD AS PLATE III

Numbers as before.

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PLATE V.—PLAN OF HEAD-VICE

The mask and ear cones are not introduced.

21. Joints connecting frontal and lateral bars (23 and 22
22. Lateral bars graduated forwards and backwards from (shown by needle), so that sliding joints can be sponding points on both sides.
23. Frontal bar.
24. Occipital bar.
25. Aural pivots, graduated.
26. Conical extremities of aural pivots.
27. Upper graduated sliding bars of temporal clamps.
28. Screw nuts running on triple thread screws. The cla in the joints (35) are pushed inwards till they are the head. The nuts are then run up and screwed ho is firmly held between the opposed clamps, the must correspond.
29. Grips of temporal clamps.
30. Upper graduated sliding bars of mastoid clamps.
31. Screw nuts of mastoid clamps.
32. Grips of mastoid clamps, points inserted on a doubly
33. Sliding joints for front feet of cage.
34. Screws to fix 33.
35. Sliding joints of temporal clamps fixed at required pos bars by screws underneath.
36. Fixed joints of aural pivots which slide in these joint with screws underneath.
37. Sliding joints of mastoid clamps fixed with screws un
38. Sliding joints of occipital bar.
39. Screws to fix 38.
40. Sliding joints for back feet of cage.
41. Screws to fix 40.
42. Circular slots for front feet of cage.
43. Circular slots for back feet of cage.
44. Screw heads to lock front feet of cage. They are ha allow cage to be applied or removed without taking
45. Screw heads to lock back feet of cage.

PLATE VI.—HEAD-VICE WITH MASK AND EAR

Plan of head-vice viewed from above, showing cones in position and illustrating their relation to head-vice.

Numbers as before.

46. Clamps to hold horizontal arms of mask in contact faces of lateral bars of head-vice.
47. Blocks with screws which can be attached to posterior bars to support the drill when in use.

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PLATE VII

Same as Plate VI, but showing cat's head in position, the skin is reflected to expose frontal sinus.

PLATE VIII

Side view of head-vice with cat's head in position.

Numbers as before.

48. Screw to fix sliding joint of temporal head clamp.
49. Screw to fix aural pivot.
50. Screw to fix sliding joint of mastoid head clamp.
51. Screws to fix frontal bar to lateral bars of head-vice.
52, 53. Removable legs of head-vice.

PLATE IX.—EXTENSIBLE SCALES

1. Scale of rectilinear needle.
2. Scale of transverse guide.
3. Scale of longitudinal guide.

55. Spiral spring enclosed in tube.
56. Tube open down one side to expose spirals of spring.
57. Screw rod attached to free end of spring.
58. Neck of tube over which milled head (60) screws and fixes rod (57).
59. Milled head which moves the spiral spring as a whole in the tube.
60. Milled head which screws over neck of tube (58) and fixes rod and spring.
61. Fine adjustment of rod and spring.
62. Ivory millimeter scale attached to tube by spring clip (63).
63. Spring clips.

PLATES X AND XIII

These two plates should be examined together and compared with Plates XI and XII.

Cage, traveling stage and vertical needle in holder. First position viewed from the front.

PLATE X

64. Horizontal frame of cage.
65. Front legs of cage.
66. Back legs of cage.
67. Front feet of cage.
68. Back feet of cage.
69. Frame of traversing stage.

PLATE XI

All parts of the stereotaxic instrument, with stage and inclined needle in sixth position. Stage applied to left face of cage. Viewed from left front. Figs. 65 and 66 should be transposed.

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PLATE XII

The whole rectilinear instrument, with stage and rectilinear needle in seventh position. Stage applied to rear face of cage. Needle facing left and viewed from left rear.

140. Switch. Movable and can be fixed to any corner of cage. It receives the two battery leads and directs the current from either, to (I) needle, (II) stop, or (III) frame of instrument as required.

PLATE XIII.—TRAVERSING STAGE

With ivory and extensible scales mounted, but without needle-holder. Viewed from above.

Comparison of these four plates will give a fairly clear idea of the cage, traversing stage, and needle-holder and their relations in various positions.

In using the terms anterior and posterior, front and back, right and left, etc., the stage is assumed to be in the first position—above the cage, the needle vertical and facing forwards. Right and left apply to the head in the frame, not to the observer.

70*a*, 70*b*. Transverse guides of traversing stage both engraved with millimeter scales. The scale on the anterior guide (70*a*) is only used in the fifth and sixth positions where the stage is applied to right or left face of cage and shows height of transverse needle above surface of frame, *viz.*, basal zero plane. The scale on the posterior guide (70*b*) is employed in all other positions. The distance of the needle is reckoned from both sides of a zero in the middle of the scale.

71. Traveling carrier of needle-holder.

72. Outer sheath of needle-holder with V-slide to receive inner sheath.

73. Pinion for longitudinal movement of traversing stage.

74. Screws for fixing longitudinal movement of traversing stage.

75. Pinion for transverse movement of traversing stage.

76. Screw for fixing transverse movement of traversing stage.

77. Quadrant for measuring inclination of needle.

78. Screw for fixing inclined needle.

79. Adjustable index on outer sheath for reading millimeter scale on left of bed of needle-holder, for use with inclined needle. Compare with Plate X.

80. Index for reading the longitudinal movement of stage on three scales: (1) Engraved scale (91) on longitudinal guide; (2) ivory scale (88) which coincides with it; and (3) extensible scale (82) between them.

81. Index for reading transverse movement of stage, on three scales at once, in the fifth and sixth positions; on the engraved scale of the anterior guide, the ivory scale and the extensible scale. In all other positions, on the engraved scale of the posterior transverse guide and the ivory and extensible scales.

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82. Extensible scale (longitudinal).
83. Extensible scale (transverse).
84. Sockets for longitudinal extensible scale.
85. Screws to hold longitudinal scale in sockets (84).
86. Sockets for transverse extensible scale.
87. Screws to hold transverse extensible scale in sockets (86).
88. Ivory millimeter scale (longitudinal).
89. Ivory millimeter scale (transverse).
90. Clamp to fix traversing stage to cage.
91. Longitudinal guides of traversing stage, one engraved with millimeter scale.
92. Millimeter scale on anterior transverse guide used in fifth and sixth positions to show height of needle above basal zero plane.

PLATE XIV.—NEEDLE-HOLDER

98. A double-barrelled insulated needle, platino-iridium and glass for stimulation or electrolysis, mounted on special bed of needle-holder with extensible and millimeter scales and electrical connections.
93. Inner sheath in which ivory bed travels by rack and pinion and carries the needle with it beyond the stop (97). The movement is read by an adjustable index (113) and the extensible and millimeter scales (111) and (112).
94. Ivory bed upon which the insulated needle (98) is fixed.
95. Head of pinion by which the ivory bed (94) is moved in the inner sheath (93) and the needle projected.
96. Head of screw by which the inner sheath (93) is locked when required in the outer sheath (Pl. XIII, 72).
97. The stop. It consists of two brass jaws lined with ivory and approximated with the tension desired by means of a screw (99).
98. Point of insulated needle.
99. Tension screw to close jaws of stop.
100. Sliding shunt by which stop can be connected with the terminal (101) for stimulation with live stop.
101. Terminal of lead (118) for bringing stop into circuit.
102. Jaws for centering and holding needle, covered with thin rubber.
103. Eccentric cams which open and shut jaws (102). The surfaces of the milled heads of the cams are marked with lines and when the lines converge at corresponding angles, the jaws are equidistant from the middle line, *i. e.*, the needle is centered.
104. Swinging arm carrying a screw which terminates in a small plate notched above to receive apex of ivory wedge (105). The object, to prevent short-circuiting, has been explained (Chapter IV, Pl. XIV, 104).
105. Ivory wedge, the apex of which is in contact with the end of the double glass tube between the wires of the needle.

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106. Terminals fixed on lower ends of brass shoes (107). Slits receive the wires of the needle which are held with screws (106).
107. Brass shoes. Numbers placed close to slots for screws which hold shoes on bed, but permit a sliding movement regulated by screw (109).
108. Terminals for battery or switch leads (116, 117) which are connected through the brass shoes with the wires of the needle.
109. Screw rods fixed by one end to the brass shoes and at the other, passing through two small drums with double-milled discs. The drums revolve in clips and are easily turned with the point of one finger and effect a fine adjustment of the sliding movement of the shoes and therefore of the wires at the point of the needle.
110. Millimeter scale of the inclined needle (it has since been lengthened to 80 mm.). It is read by an adjustable index on the outer sheath (Pl. X, 79) and shows the distance of the point of the needle from the pivot by which the outer sheath is attached to the carrier in the traversing stage. A measurement always employed with the inclined needle.
111. Extensible scale.
112. Ivory millimeter scale. These are scales of the rectilinear needle. When in use a selected spiral is made to coincide with zero of the ivory scale. The index reads the number of spirals and the number of millimeters together. A stop scale is marked on both sides on the adjacent borders of the inner and outer sheaths. It shows the distance in millimeters of the extremity of the stop from the zero plane to which it is perpendicular and is a constant, *i. e.*, a measurement of the instrument. If the needle is racked down till its point coincides with the extremity of the stop and the adjustable index (113) is made to read the same on the ivory scale (112) as the stop scale, that figure must show the distance of the point of the needle from the zero plane in millimeters and the index at the same time shows the number of spirals or coordinates on the extensible scale (111).
113. Adjustable index which reads both scales of the rectilinear needle together.
114. Slide which carries adjustable index (113).
115. Screw to regulate friction of pinion (95).
116, 117. Positive and negative leads from battery or switch to needles.
118. Lead from battery or switch to terminal (101) connected with stop (97) by shunt (100).

PLATE XV.—INSULATED NEEDLES

Three forms of platino-iridium needles insulated in glass tubes, actual size and enlarged.

1. Single needle.
2. Double-barrelled needle.
3. Concentric needle.

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PLATE XVI.—CUTTING NEEDLES AND BEDS

I. Pilot Needle and Bed

1. Pilot needle.
110. Indicator scale for inclined needle.
113. Index for rectilinear needle.
114. Slide for adjusting index (113).
118. Screw head serving as handle for introducing pilot needle.
120. Clamp which holds pilot needle.

II. Cyclotome and Its Bed Fitted Into Inner Sheath

1. Shaft of hollow needle.
2. Cylinder which fits into clamp (119).
3. Milled disc which rotates needle (1).
4. Cylinder graduated in millimeters read by lower edge of (5); shows distance concealed knife (7) is projected.
5. Cylinder which screws down over (4) on which its lower edge serves as index to read graduation. It is rotated by milled disc (6) and carries a wire which passes down hollow needle (1) and is connected with concealed knife (7) which it projects.
6. Milled disc which rotates cylinder (5).
7. Watch-spring concealed knife which can be projected 4 mm. and withdrawn by rotating (6).
9. Milled disc which with (3) fits the clamp (119) and prevents any longitudinal displacement of needle.
118. Screw head which serves as handle.
119. Clamp which holds cylinder (2) with moderate friction effected by screw (121); it checks but does not prevent rotation of cylinder.
121. Screw which holds clamp (119) and regulates friction.

The following parts seen in this figure are also shown in Plate XVI, 114, and have the same numbers.

93. Inner sheath.
95. Head of pinion by which bed is moved in inner sheath.
96. Screw by which inner sheath is locked in outer sheath.
97. Stop.
99. Tension screw to close jaws of stop.
100. Shunt for bringing stop into circuit.
101. Terminal of lead for connecting stop.
110. Scale of inclined needle.
113, 114. Adjustable index for scales of rectilinear needle.
115. Screw to regulate friction of pinion (95).

III. Orthotome

Numbers as in II.

8. Wire which is connected with concealed knife (7).

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IV. Mussen's Spherotome

Numbers as in II.

V. Fine Steel Tube

For introducing drugs, etc.

1. Tube.
2. Cylinder held by clamp (119).
10. Funnel.
11. Rod which fits tube (1).

PLATE XVI A

Design for improved bed for cutting needles, especially fine hypodermic needles from which a steel wire can be projected at a right-angle for 2 or 3 mm.

1. *Bed* which is made of brass and fits the inner sheath (Pl. XIV, 93) of the needle-holder. The rack shown on the edge of the bed is engaged by the pinion (95) attached to the inner sheath and serves to project or withdraw the needle.
2. *Adjustable index* for reading the scale of the needle in the rectilinear instrument.
3. *Indicator scale* for inclined needle.
4. *Screw head* which serves as a handle for introducing or removing bed (1) from inner sheath (93).
5. *Outer Cradle.*
6. *Inner Cradle.*
7, 8. *Upper and lower end plates* of outer cradle.
9, 10. *Upper and lower end plates* of inner cradle.
11. *Rectangular center rod* pivoted in the slots of the upper and lower end plates of outer cradle. It traverses the inner cradle from one end plate to the other and is fixed to both. It therefore supports the inner cradle and when rotated on its pivots effects a rotation of the inner in the outer cradle. The center rod has a circular groove at the point where it engages the slot (13) of the upper end plate (7) to facilitate rotation of the rod and prevent its longitudinal displacement.
12. *Cross handle* attached to end of center rod. The four arms, corresponding to the four surfaces of the rod and inner cradle, indicate quarter turns of the latter.
13. *Slot* in upper end plate of outer cradle. It engages the circular groove in the center rod (11).
14. *Spring bar* which holds center rod (11) in the slot (13) of upper end plate.
15. *Spring* to hold (14).
16. *Screw thread* which occupies a few millimeters of the center rod (11) and on which the milled disc (17) moves the clamp (18).

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17. *Milled disc* which travels a few millimeters up and down (16) carrying the clamp (18) and wire (19) with it.
18. *Sliding clamp* in which the end of the wire (19) is fixed. A circular groove at the upper end of the clamp is engaged by a corresponding feathered edge on the lower surface of the milled disc (17). Rotation of the disc does not turn the clamp, owing to the square section of the center rod on which it slides, but causes it to travel up and down the center rod as far as the milled disc (17) moves on the screw (16).
19. *Wire* which passes down hollow needle (29) and is continuous with watch-spring knife (19) which it causes to project from the slot near the end of the needle.
20. *Slot in clamp* (18) to hold wire (19).
21. *Ring* which screws over tapered nozzle (22) of sliding clamp (18) causing the slot (20) to grip the wire (19).
22. *Tapered end of sliding clamp* provided with screw thread for ring (21) which makes a vice of slot (20) to hold wire (19).
23. *Index of millimeter scale* (24) showing length of wire or knife (19) projected from needle (29).
24. *Millimeter scale*, adjustable.
25. *Hollow tapered nozzle* screwed to lower end plate (10) of inner cradle (6) which engages the socket (26) of the needle; nozzle of different sizes for different needles can be employed and interchanged.
26. *Socket of needle.*
27. *Stud* which engages slot (28) in socket (26) of needle prevents displacement and ensures the projection of the wire or knife in the same direction.
28. *Slot in socket* (26) *of needle* for stud (27).
29. *Shaft of needle.*
30. *Orifice* from which knife or wire (19) is projected from needle.
31. *Slot in lower end plate* (8) to receive the needle which thus forms the lower pivot on which the inner cradle rotates.
32. *Cross bar* with V-shaped notch on posterior edge to engage the needle (29) and hold it in slot (31).

PLATE XVII.—DRAWINGS OF THREE CUTTING NEEDLES

The three following needles all fit the same bed as (II).

VI. Vertical Cyclotome

For making circular or disc-shaped incisions with a sheathed knife in a plane parallel to the axis of the needle.

III. Orthotome

For making small incisions with concealed knife in the same direction as the needle and parallel to it.

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IV. Mussen's Spherotome

For cutting small spheroids with concealed knife.

These needles have been explained (Chaps. I and IV).

PLATES XVIII, XIX, XX, XXI

These four plates show the instrument with a cat's head in position and the needle applied in the first, sixth and seventh positions.

The parts have not been numbered, as they have all been described in previous plates.

PLATES XXII, XXIII, XXIV.—THE NEEDLE-GAUGE

These three plates illustrate the needle-gauge which was used with the rectilinear machine originally and which will meet the requirements of those who have that machine, but have not procured the drilling and gauging cage (Pl. XXXIV). The gauge shown in these plates was constructed before the three diameters of the cage had been made identical, so it is provided with an adjustable index and a scale to set it and the figures for the three diameters of the cage are engraved on one of the feet (132). In future the adjustable index and extra scale will not be required. The index (142) will be at zero on scale (135) when the point of the needle or cap (138) is at the zero plane perpendicular to the needle. In all other respects the application of the gauge will be the same as that shown in the plates. In Plates XXIII, XXIV, the gauge is shown applied to the cage for measuring the vertical diameter of the head. In Plate XXIII the adjustable index (139) is at zero on the scale (135), the index (142) having been brought to 52 on the scale (134). This being the figure engraved at (132) for vertical measurement, the point of the needle is seen at the interaural line. (Pl. XXIV) shows the gauge applied to the head in the cage, the needle penetrating the integuments is in contact with the surface of the cranium and the adjustable index reads 30, showing that in the frontal zero plane, in the mid-sagittal line, the distance from the interaural line to the vertex is 30 mm. in this head.

The cylindrical needle gauge (Pl. XXXIV, 26), which is used with the drilling and gauging cage (Pl. XXXIV) and which fits the same slots as the drill guides (7 and 8) is applied in the same way. When the point of the needle is at the zero plane to which it is perpendicular the index reads zero on its scale, and when the point of the needle is in contact with the cranium, the scale shows the number of millimeters between the zero plane and the point of contact, *i. e.*, the required dimension.

Numbers on cage and head-vice as before (see Pls. VI and X).

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131. Base bar.
132. Feet. Right and left.
133. Slide block which travels on (131).
134. Millimeter scale for setting adjustable index (139).
135. Scale for measuring depth of needle.
136. Graduated gauge ending in needle (137) and cap (138). (Figures placed on screw for cap.)
137. Measuring needle, the point of which must be flush with cap (138).
138. Cap which covers needle. When screwed home the point is level with that of the needle and measurements can be reckoned from either.
139. Adjustable index set at zero when the index (142) is at the number on the scale (134) required for the dimension to be measured and engraved at (132). Not required in future.
141. Screw to fix adjustable index (139).
142. Index of slide block (133).
143. Screw to fix slide block (133).

PLATES XXV-XXIX.—INDICATORS

The plates illustrate the two- and three-dimensioned indicators with an arrangement of adjustable gratings for making corrections for size.

The pattern with a ruled card described (Chap. III) has not been constructed, but by comparing the description with these plates the nature of the modification will be evident. When the two-dimensioned indicator was constructed, some difficulty was experienced in making gratings of which the spaces between the threads were rather less than 1 mm. The purpose of the instrument is served equally well if it is enlarged so that in every part as well as the gratings nominal millimeters actually measure two. This makes the instrument inconveniently large if the gratings represent a whole lamella, but as the objective point must lie in one of the quadrants formed by the crossed zero lines of a lamella, it is sufficient if that quadrant only is represented. To represent any quadrant in any lamella in three dimensions the position of the instrument and of the zero lines must be variable; the bars, therefore, which define the zero lines are adjustable and it will be found that by changing the position of the instrument and adjusting the bars, any quadrant can be represented. In future it will be more convenient to make the gratings with spaces of only 1 mm. and representing a whole lamella, the zero lines will then be constant and the adjustable zero bars unnecessary. The plan has generally been followed of illustrating instruments which have been constructed and used and there is some advantage in showing alternative methods which are practicable even if they are not adopted.

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PLATE XXV.—ADJUSTABLE GRATINGS FOR TWO-DIMENSIONED INDICATOR

The gratings are formed of silk threads stretched between opposing pairs of sway bars. The threads are in groups of five, alternately black and white. The spaces between the threads are set to measure 2 mm., or more, or less, by inclination of the sway bars (3, 3) (4, 4), which can be fixed at any point by a quadrant and screw (5, 6). The threads pass round small pegs arranged at equal distances on the bars. Each pair of bars is kept taut by a spring and tension screw (7, 8).

1. Vertical threads of grating.
2. Transverse threads of grating.
3, 3. *Pivoted* sway bars for vertical threads.
4, 4. *Pivoted* sway bars for transverse threads.
5. Quadrant with screw for fixing vertical pair of sway bars.
6. Quadrant with screw for fixing transverse pair of sway bars.
7. Spring and tension screw for vertical threads. See Pl. XXVI.
8. Spring and tension screw for transverse threads.
9, 9. Screw nuts which receive and fix sliding plates of frame of indicator (Pl. XXVI, 10).

PLATE XXVI.—THE TWO-DIMENSIONED INDICATOR (COMPLETE)

The various parts of the grating already shown (Pl. XXV) can be seen beneath the frame which carries the quadrant and needle, zero bars and scales. For convenience, the whole instrument and all the scales are enlarged in the proportion of 2: 1. Nominal millimeters, therefore, measure 2 mm., but, as the enlargement is proportional, the scales in the indicator correspond with those of the stereotaxic instrument, though in the latter the scales are in actual millimeters. For the purposes of description the indicator is assumed to be in the first position of the needle in the stereotaxic instrument, *i. e.*, the quadrant above, facing forwards, the needle inclined in the direction of the right internal capsule downwards and to the left (the observer's right).

10. Frame.
11. Plates by which the frame is held on the board by the screw nuts (9, 9). When these are relaxed, the whole frame can slide on the plates.
12. First zero bar, representing one of the zero planes. It always represents the zero plane parallel to the traversing stage in the stereotaxic instrument, perpendicular to the rectilinear needle, and as that is a constant, the distance from this bar to the pivot of the needle (21) is a constant in the indicator, and if the bar is moved, the frame and the needle move with it.
13. Second zero bar (*a*).

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14. Second zero bar (*b*).
The objective po
measured from two
The first zero bar (
for different positio
indicator to repres
together, and whicl
second zero plane, s
cannot be distingui
adopted for that pu
15. Is placed on the quadr
on which the quadr
slides on the guide
16. Index for reading quad
17. Sheath in which needl
18. Quadrant scale.
19. Screw which fixes carri
20. Finder needle.
21. Pivot. The pivot itsel
the index for read
point to pivot in m
22. Pointer at the end of n
23. Screw to fix needle in
24. Transverse guide. C
stereotaxic instrun
25. Upper millimeter scal
which moves with
to be moved to co
because the object
grating from it. 1
measures the dist
zero bar, should m
zero bars move wit
the pivot and fram
26. Lower millimeter scal
moving with it.
27. Index which reads sc
tance of pivot (21)
28. Finder needle and its
of second zero bar
29. Pins to fix first zero
removed.
30. Screw to fix needle in

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PLATES XXVII-XXIX.—THE THREE-DIMENSIONED INDICATOR

1. Steel base plate.
2. Right and left anterior columns with slots for feet of cage or equatorial corresponding to similar slots (42) in the head-vice (Pl. VI).
3. Posterior ditto.
4. Longitudinal horizontal grating for transverse measurement. It is composed of silk threads about 1 mm. apart, the spaces being variable by inclination of the sway bars (5).
5. Sway bars of longitudinal grating (4).
6. Quadrant with scale to adjust longitudinal grating (4).
7. Screw to fix quadrant (6).
8. Transverse grating, prefrontal.
9, 9. Sway bars of (8).
10. Quadrant and scale for adjusting transverse grating (8).
11. Screw to fix (10).
12. Transverse grating, postfrontal.
13, 13. Sway bars of (12).
14. Quadrant and scale for adjusting transverse grating (12).
15. Screw to fix (14).
16. Vertical grating.
17, 17. Screws to fix vertical grating to plate (1).
18. Bridge which supports horizontal radius bar (23).
19. Rotatory and sliding joint of horizontal radius bar (23).
20. Screw to fix joint (19). The figure is placed over the pivot of the rotatory joint.
21. Graduated quadrant for adjusting rotatory joint (19).
22. Pinion for racking horizontal radius bar (23) in joint (19).
23. Horizontal radius bar.
24. Vertical index needle.
25. Sliding joint and fixing screw of vertical index needle (24).
26. Pinion for racking vertical radius bar (27) in joint (30).
27. Vertical radius bar.
28. Sliding joint and screw of horizontal index needle (29).
29. Horizontal index needle.
30. Rotatory and sliding joint of vertical radius bar (27).
31. Screw to fix joint (30).
32. Sway bars of vertical grating.
33. Quadrant of vertical grating.
34. Screw to fix quadrant (33). (*N. B.*—The quadrant of the vertical grating was not completed when the other plates were prepared.)

White threads will be noticed at intervals in all the gratings; they represent all the standard dimensions in the cat and rhesus and facilitate direct measurement whether this is adopted as the sole method or to verify measurements by the quadrant scales.

In the longitudinal horizontal grating the central white thread represents the median longitudinal plane. Of the pairs of threads

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parallel to it the inner pair represent the standard transverse diameter of the cranium of the cat, the outer the same dimension of the rhesus.

In the transverse horizontal grating a white thread at the junction of the anterior and posterior gratings represents the interaural line, and four other threads the corresponding anterior and posterior dimensions in the same standard animals.

Three white threads in the vertical gratings represent from below upwards the basal horizontal plane and the standard vertical measurement of the cranium in the cat and rhesus, respectively.

PLATE XXVIII A

A method of identifying and representing the index point.

1. Square rod sliding vertically without rotating in the slot at the end of the horizontal radius bar (23) and fixed by a screw. It is reversible.
2, 3. Horizontal arms carrying rotating crosses, the pivots of which represent index points (4, 4′; 5, 5′).
4, 5. Index points. Upper and lower. Numbers point to upper ends of tubes.
4′, 5′. Lower ends of tubes which may serve as index points.
6, 7. Arms of crosses.
8. Needle which passes vertically through the pivots or naves of the crosses and identifies a marked mesh in the horizontal grating.

PLATE XXIX.—THE EQUATORIAL APPLIED TO INDICATOR

Shown in position mounted on the indicator and carrying the needle-holder (Pl. XIV) and operating needle (98), the point of which is in contact with that of the index needle (24) of the indicator. Numbers in the indicator as before.

35. Inner ring of turntable fixed by four feet (37, 38) which are engaged in the slots of columns of the indicator (2 and 3).
36. Outer ring of turntable which rotates on (35) and is fixed by screw (39).
37. Anterior feet of inner ring (35).
38. Posterior ditto.
39. Screw to fix turntable.
40. Arch which passes across the outer ring and conveys the needle-carrier (44) which traverses it by a sliding movement controlled by a fixing screw (45).
41. Rectilinear guides on which the feet of arch slide, carrying the arch and needle-holder across the rings of the turntable at right-angles to the direction of the arch.

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42. Feet of the arch which slide on (41).
43. Screw for locking sliding movement of arch.
44. Carrier on which is pivoted the outer sheath (72) o
traverses the arch (40) and is fixed at any req
screw (45).
45. Screw which fixes the carrier (44) and also the qua
sheath (47).
46. Screw which locks the inclination of the outer she
carrier (44).
47. Quadrant connecting carrier (44) with outer shea
lates the inclination of the outer sheath and ne
carrier and quadrant.
48. Screw which locks the inclined movement of the ou
quadrant (47).

PLATE XXX.—THE EQUATORIAL APPLIED TO
FRONT VIEW

When the equatorial is applied in this way
which contains a head, the latter is encircled
about the level of the mid-horizontal plane. It
this affords the needle a great variety of positi
Numbers of equatorial and head-vice as in Pl

PLATES XXXI, XXXII, XXXIII AND XXXIV.—D
GAUGING

These three plates show the method of drilling
first adopted in the rectilinear machine and w
means of a square frame, one side of which is re
can be fitted over the cage in the frontal a
planes. The former position is employed for
verse and the latter for longitudinal drilling. T
the frame (2 and 3) carry slide blocks (5 and 6)
for sliding cylindrical drill guides (7 and 8) w
into contact with the head and retained in any
(10 and 12). The slide blocks (5 and 6) can a
point on the side of the frame to which they a
screws (9 and 11) and the position of the sli
mined by a millimeter scale and an index forme
edge of the slide block.

The three punctures usually required for verti
drilling are all made in the frontal zero plane,
used for these purposes is retained in the front
longitudinal drilling the frame, which is now fi
in the horizontal plane (Pl. XXXII), is brou

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The numbers indicating parts of the head-vice and cage as before; those referring to parts of the drilling apparatus are as follows:

1, 2, 3, 4. The four sides of the frame which is applied to the cage. The side (4) is detachable and fits on to (2 and 3) by joints (13 and 14). The sides (2 and 3) carry slide blocks (5 and 6). The slide blocks are adjusted by millimeter scales and indices and fixed with the screws (9 and 11). They are also perforated with slots to fit the sliding cylindrical drill guides (7 and 8) and the latter are fixed by the screws (10 and 12).

5, 6. Slide blocks for drill guides, attached to sides 2 and 3 of frame.

7, 8. Cylindrical drill guides.

9, 11. Screws to fix (5 and 6).

10, 12. Screws to fix (7 and 8).

13, 14. Joints for fixing detachable side of drilling frame.

15, 16, 17, 18. Clamps for attaching the drilling frame to the ordinary cage of the rectilinear machine.

19. Screws for adjusting the height of the frame in the horizontal position for longitudinal drilling.

32. Needle passed through opposite pairs of drill guides.

In Plates XXXI to XXXIII, except 32, all numbers above 20 are numbers previously applied to parts of the head-vice and cage (see Pls. VI and X) and refer to the same parts in these plates.

Pl. XXXIV.

1, 2, 3, 4. Sides of frame permanently attached to cage for vertical and transverse drilling and gauging.

5, 6. Slide blocks for vertical drill guides or cylindrical needle-gauge.

7, 8. Drill guides shown here in the position for longitudinal drilling and traversed by a needle (32).

9, 11. Screws to fix slide blocks (5 and 6).

10, 12. Screws to fix drill guides (7 and 8) or needle-gauge (26).

13, 14. Joints for attaching removable bar (4) of drilling frame.

15, 16. Anterior and posterior transverse horizontal bars which are raised or lowered by slide blocks (21 and 22) on the anterior and posterior legs of cage and carry slide blocks (17 and 18) perforated for drill guides for longitudinal drilling. The slots also fit the needle-gauge.

17, 18. Slide blocks carrying guides for longitudinal drilling.

19, 20. Screws to fix (17 and 18).

21, 22. Terminal sliding joints of horizontal bars (15 and 16). The joints are raised and lowered on the legs of the cage, adjusted by millimeter scales and fixed with screws.

23. Slide blocks which can be raised and lowered on the sides (2 and 3) of the frame attached to the cage. The blocks are perforated for drill guides for transverse drilling and for needle guage.

24. Screws to fix (23).

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25. Screws to fix drill guides (7 and 8) or needle-gauge (26) in blocks (23).
26. Cylindrical needle-gauge.
27. Screw cap of needle-gauge. For measuring the surface of the cranium the needle is made flush with the cap by the screw (28) and the cap is then removed.
28. Screw for projecting or withdrawing needle of gauge and making it flush with the cap.
29, 30. Screws to fix (21 and 22).
31. Needle in slots of blocks for transverse drilling.
32. Needle in slots of blocks for longitudinal drilling.
33. Needle of cylindrical gauge. Projected by screw (28).
34. Depth gauge. For measuring posterior wall of orbit (Chap. VI).
35. Cross bar of gauge (34).

PLATE XXXV

Figure I

Galvanic plug for arresting hæmorrhage from bone after trephining.

1. Expanding copper collar. It fits the trephine hole loosely until it is expanded by drawing up the ivory cone (2).
2. Ivory cone which expands the collar (1).
3. Copper ring grooved on its under surface and packed with moist wool. It rests on the surface of the cranium encircling the trephine hole and by the counter-pressure of the cone and collar exerted through the bridge and screw is kept in firm contact with the bone.
4. Screw which draws ivory plug (2) and expands collar (1).
5. Ivory bridge for maintaining counter-pressure between collar (1) and ring (3), thus making the plug self-retaining.
6. Screw which draws collar (1) up and presses bridge (5) down.
7. Terminal connecting battery lead with collar (1).
8. Lead connected by terminal which is not seen, with copper ring (3).

Figure II

Nickel self-retaining plugs for keeping fine glass or platinum tubes in the brain.

1. Plug which screws into trephine hole.
2. Tube which fits the glass or platinum tube to which it is fixed with a drop of shellac. A small disc at the lower end of this tube fits the hollow plug (1).
3. Glass or platinum tube.
4. Screw perforated for the passage of the glass tube fits the hollow plug (1) and when screwed down holds the nickel tube (2) and the glass tube within it in place, and at the same time projects only slightly above the surface of the bone.

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In practice the parts 1, 2, 3, 4 in the position shown are all slipped over a fine pilot needle fixed in the holder, and so introduced into the trephine hole by the stereotaxic mechanism. The pilot and glass needles are directed to the required point in the brain. The plug (1) is screwed into the trephine hole, the tube (2) is then slipped down till the disc rests in the bottom of the hollow plug, when it is sealed to the glass tube with a drop of hot shellac.

Finally the cap (4) is screwed down, leaving the end of the glass tube projecting externally.

FIGURE III

These trephines fit the handle of a dental engine; they are provided with adjustable stops (2), which are convenient, as the average thickness of bone at any point can be judged approximately from the charts.

The second form is the best, as it will in future be fitted with a small locking screw. If it has not quite penetrated the bone it can be lengthened a turn or two at a time and reintroduced and the crown of bone separated without risk of wounding the dura. As the trephines can be changed very quickly in the handle, it is best to begin with one with a fixed center pin until a groove is cut and then substitute one with a stop but no pin.

PLATE XXXVI.—QUADRANT CALCULATOR

The use of this is explained in Chapter VII.

1. Vertical scale or table.
2. Sector or inclined scale.

STEREOTAXIC INSTRUMENT FOR SPINAL CORD

(PLS. XXXVII, XXXVIII AND XXXIX)

A stereotaxic instrument for introducing insulated needles for electrolysis or stimulation of small areas, or tracts in the spinal cord.

PLATE XXXVII

Shows the instrument from the front with the balance gauge in position. The object of the gauge is to set the sheath by the quadrant, so that either the pilot or the insulated needle will be perpendicular to the zero horizontal line, which lies on the surface of the posterior columns of the cord in a transverse section.

PLATE XXXVIII

The same from the right front with the pilot needle in position.

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PLATE XXXIX

The same with the insulated needle in position.

1. Cradle.
2–5. Levers with spring back and pinion catches for gripping vertebra.
6. Screw for transverse movement of stage.
7. Screw to fix needle-holder which slides in sheath (23).
8. Quadrant for setting sheath by balance gauge (9).
9. Balance gauge.
10. Millimeter scale for transverse movement of stage effected by screw (6).
11. Pilot needle.
12. Screw for longitudinal movement of needle parallel to axis of spine.
13. Needle-holder.
14. Ivory bed of needle-holder.
15. Clamp for glass tube of insulated needle.
16. Clamp for wire of insulated needle.
17. Terminal for battery wire.
18. Wire and glass tube.
19. Scale for showing distance of point of needle from transverse zero line on surface of posterior columns.
20. Adjustable index for scale (19).
21. Vulcanite stop which is brought into contact with posterior columns of cord.
22. Fine screws for extension of bed and needle measured by scale (19) and adjustable index.
23. Sheath of needle-holder.

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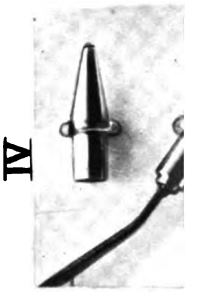

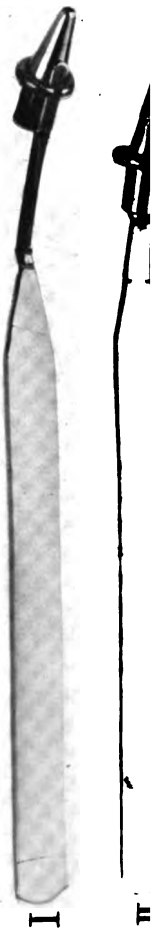

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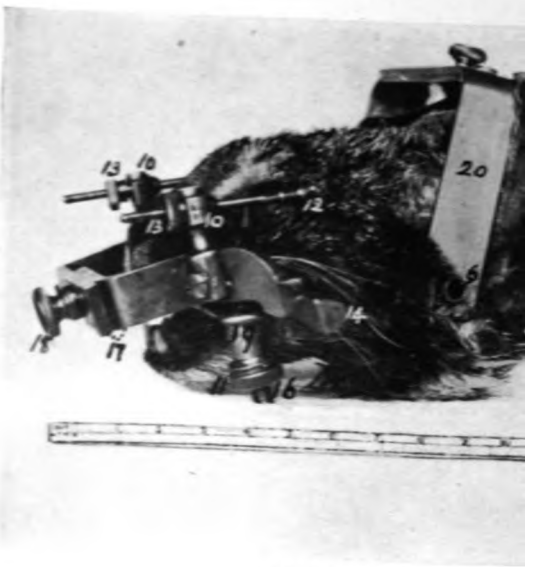

PLATE III.

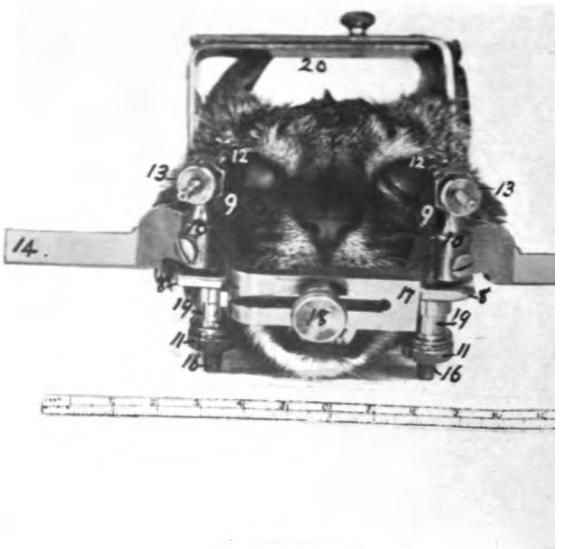

PLATE IV.

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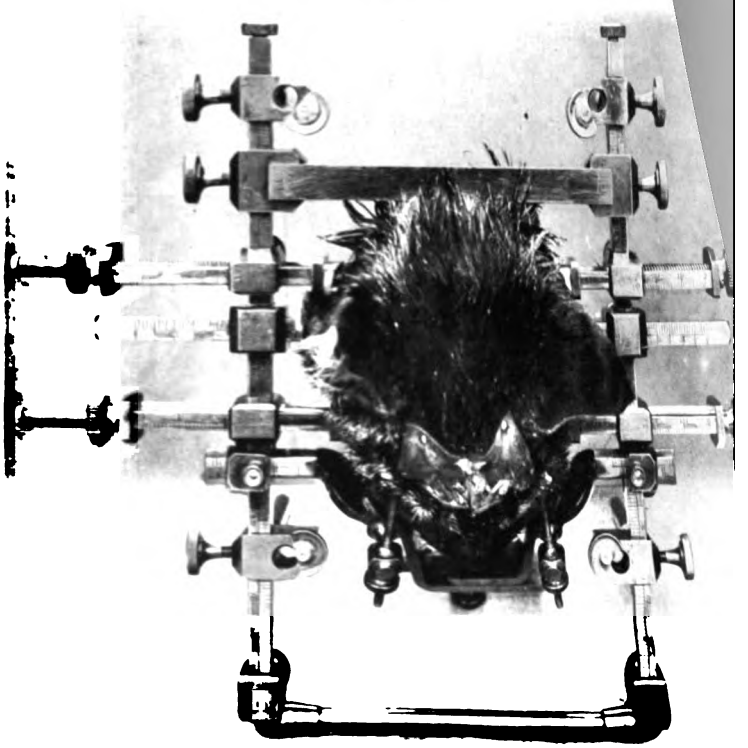

PLATE VII.

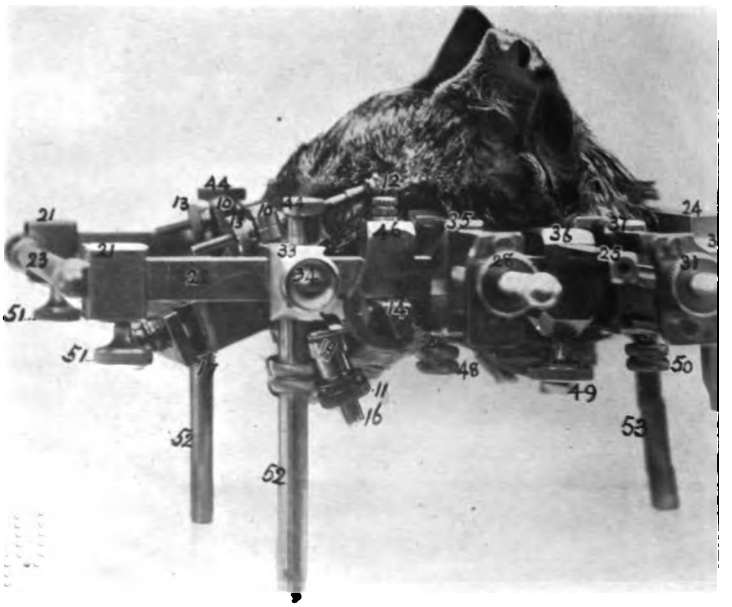

PLATE VIII.

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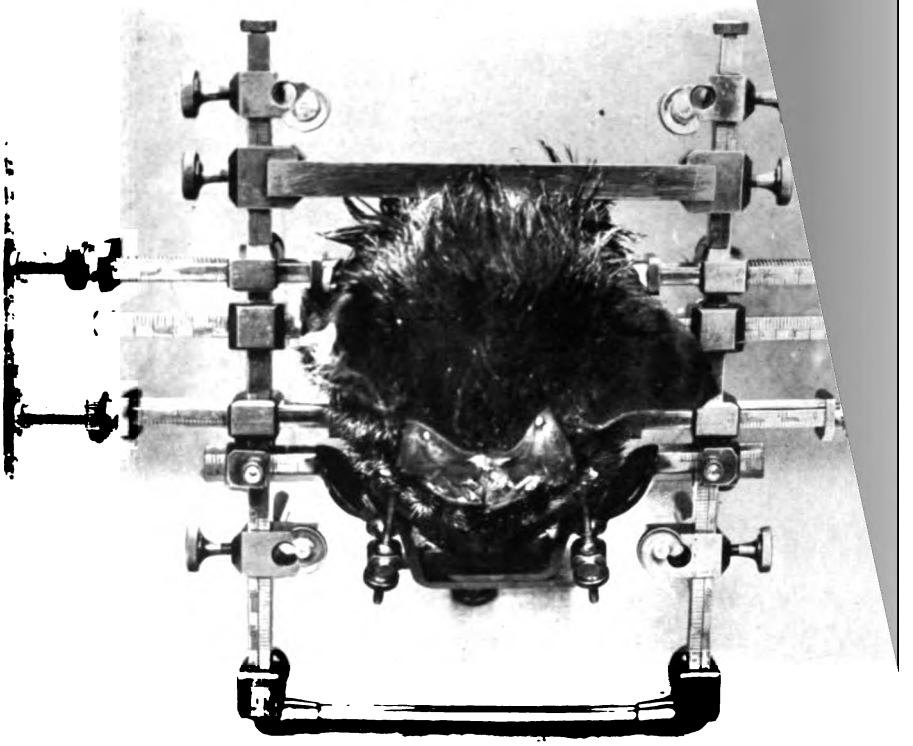

PLATE VII.

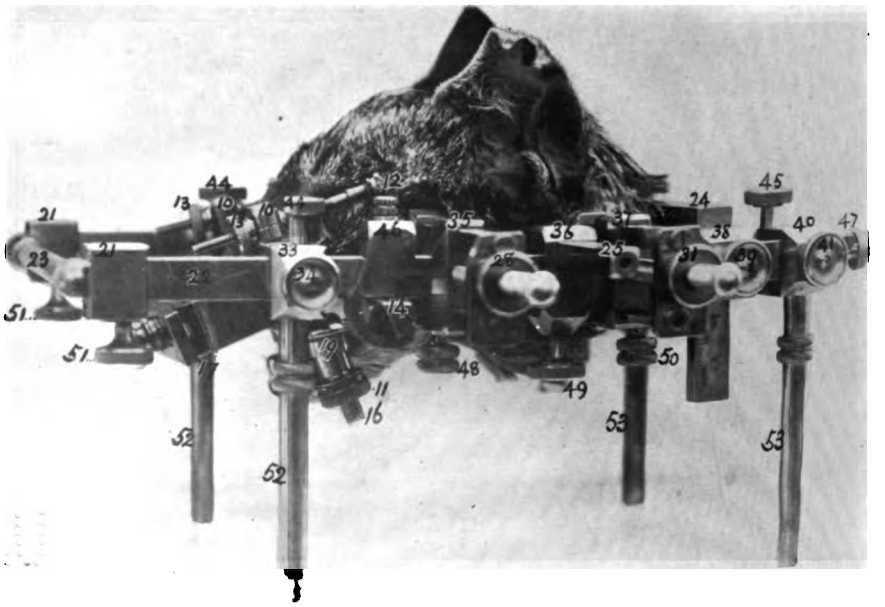

PLATE VIII.

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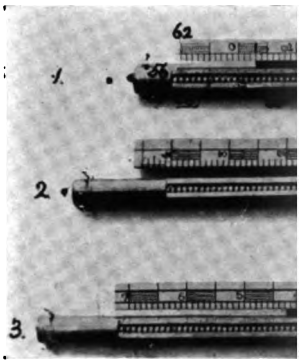

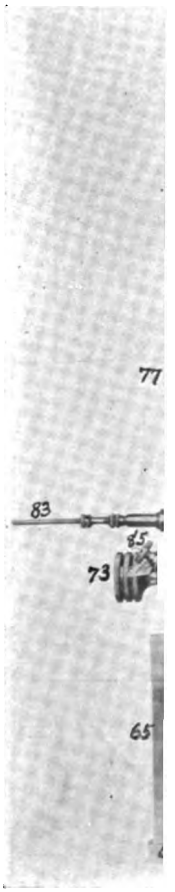

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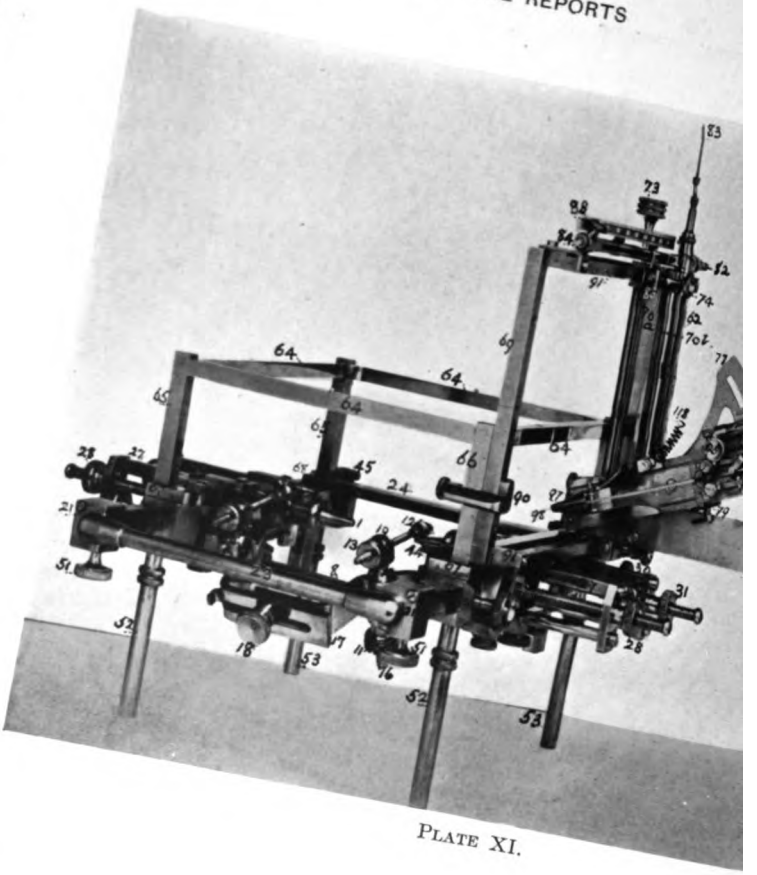
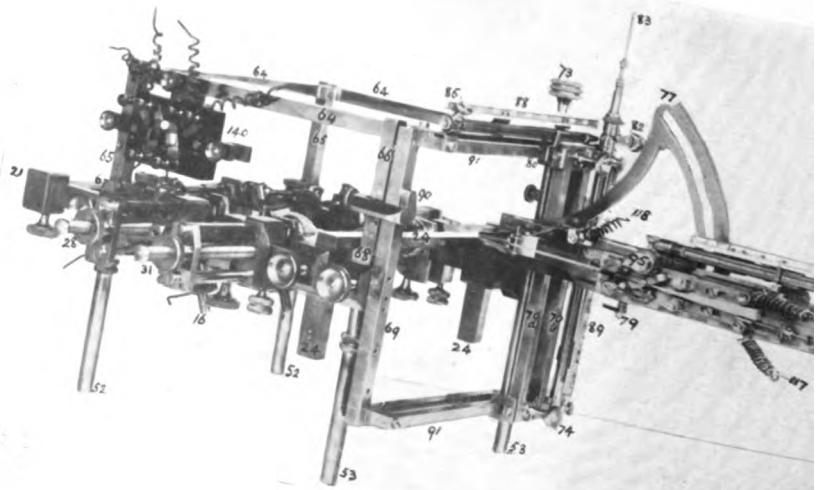


PLATE XI.



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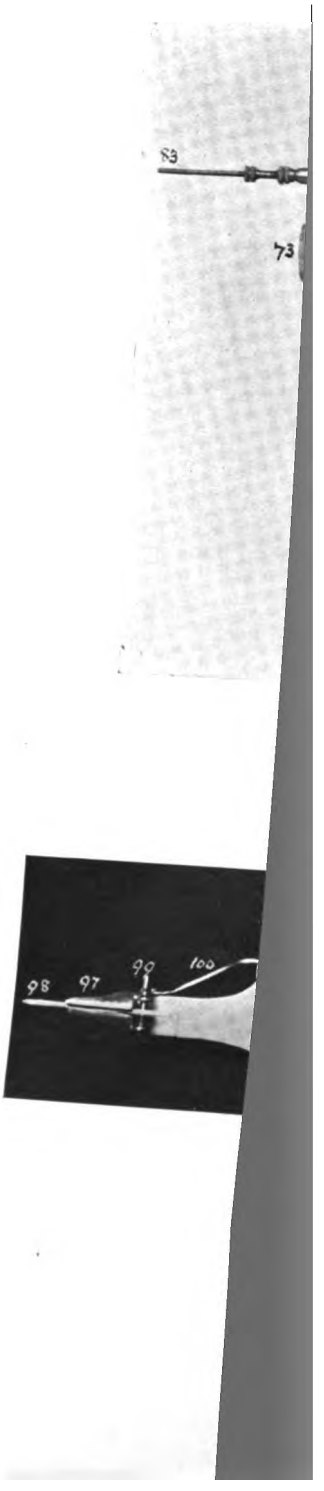

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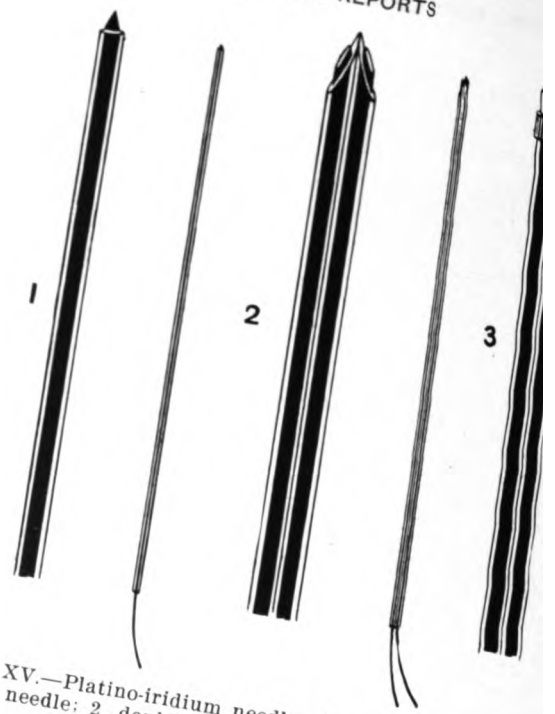

PLATE XV.—Platino-iridium needles insulated in glass tube
needle; 2, double-barrelled needle; 3, concentric ne
(Actual size and enlarged.)

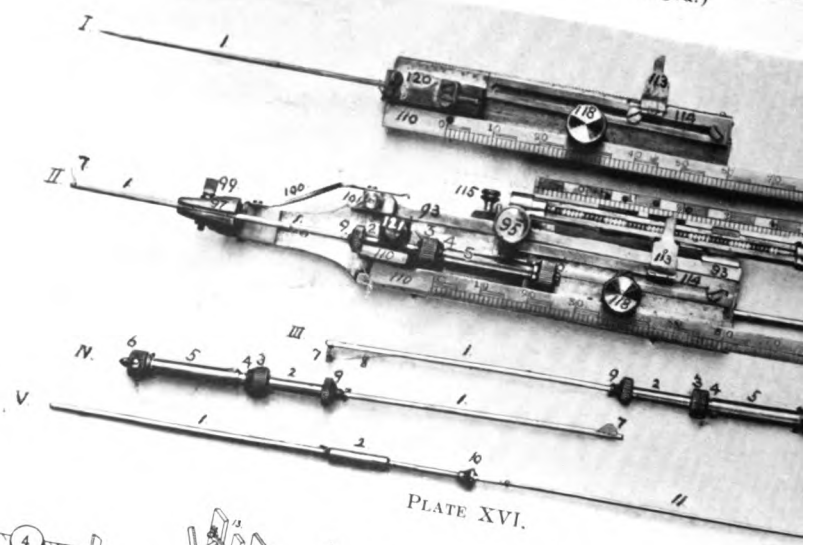

PLATE XVI.

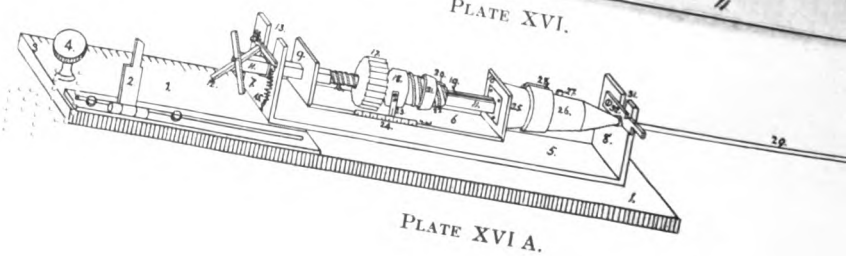

PLATE XVI A.

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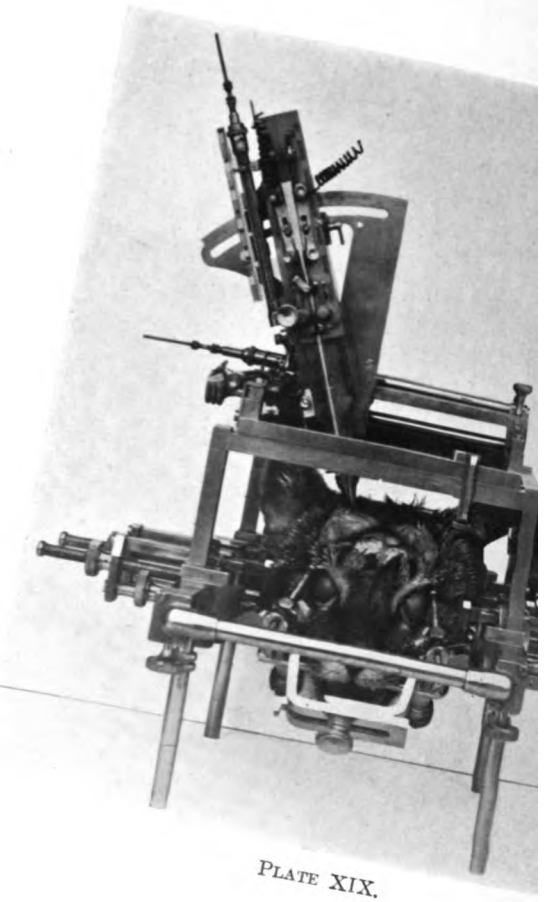

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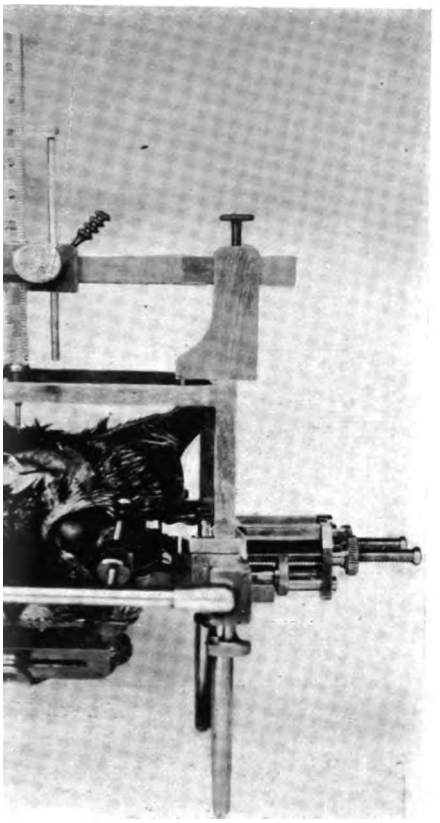
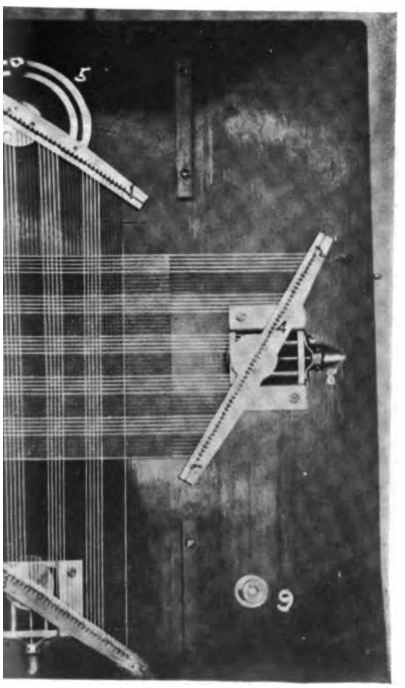


E XXIV.



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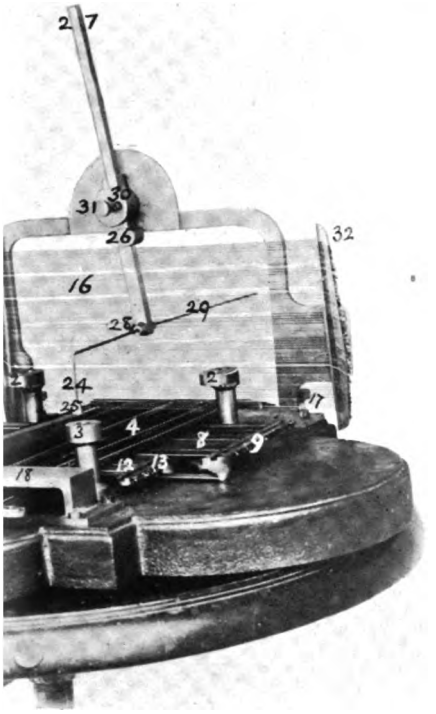

E XXVIII.

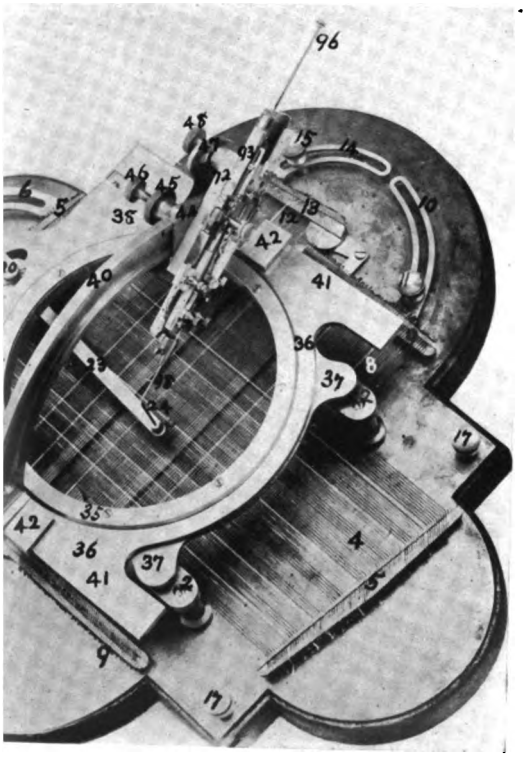

PLATE XXIX.

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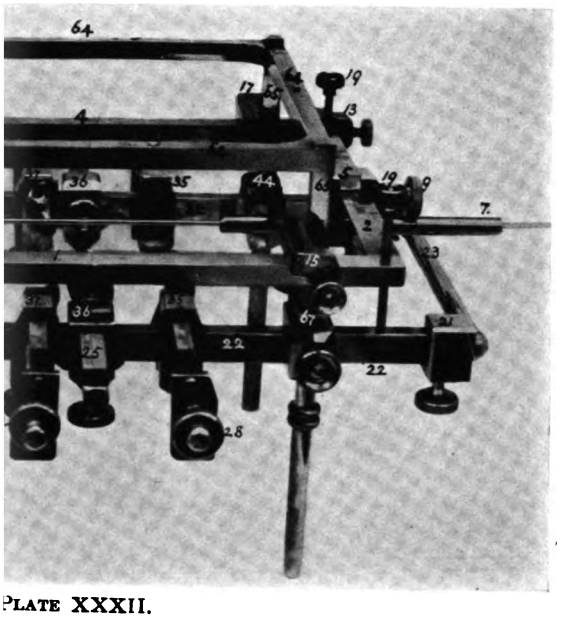
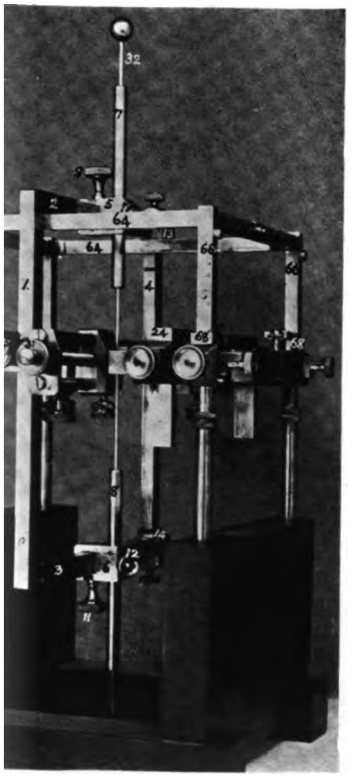


PLATE XXXII.



LATE XXXIII.

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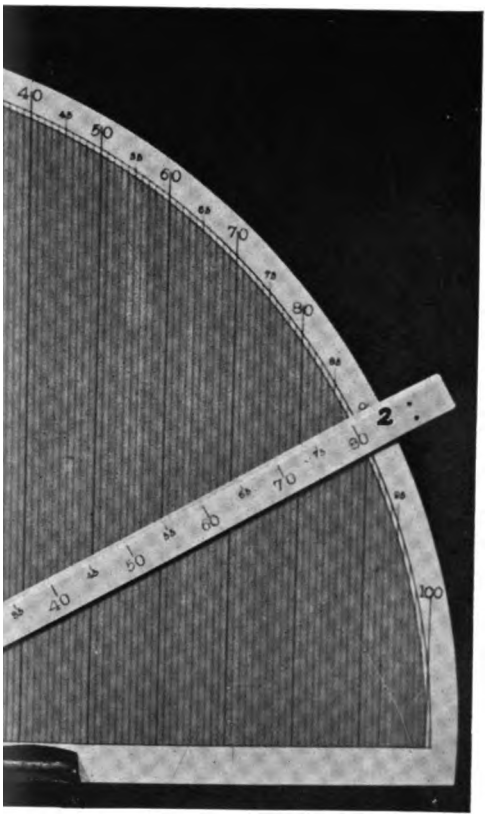

PLATE XXXVI.

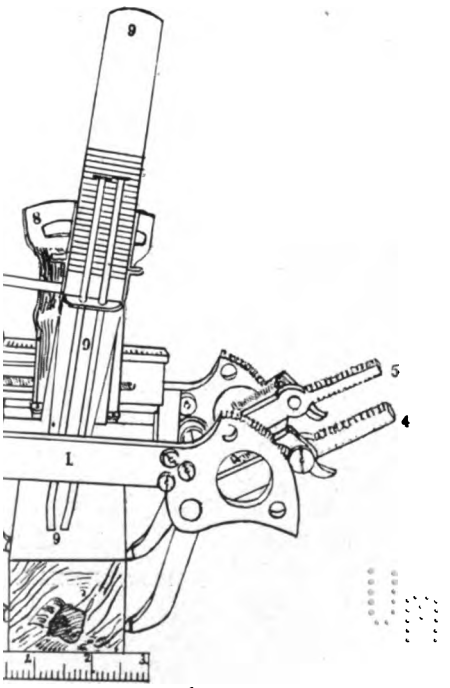

PLATE XXXVII.

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Part II

phs of Sections of the Frozen
f the Monkey and Cat

the Rhesus Monkey (*Macacus*)

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graphs of frontal sections of the cranium
the third part of an atlas of which the
ng sagittal and frontal sections of the cat,
y before the war as supplements of the
l Neurologie. The third part was nearly
enced and would shortly have appeared in
ourse all arrangements were interrupted
itely postponed, and the course of events
ersion to this arrangement exceedingly
istances we were glad to avail ourselves of
of The Johns Hopkins Hospital, Balti-
er in the United States. The use of the
method of which they form an essential
rst number of the atlas. This may not be
ject is discussed in detail in a description
l instruments published in the same cover
ig a repetition of the explanation unneces-
te here that the sections represented are
oximately one millimeter thick; the head
ith a saw parallel to one of the three zero
m is divided for topographical purposes;
rpendicular to the first, are shown in each
, and these together with the number of
, in every chart for identifying any cubic
e photographs are enlarged two diameters
is of size in three dimensions are effected
l scale with the saw and the addition of
limensions of the chart photographs, when
m near the average size is adopted for each
in the standard all the divisions are milli-
ow the standard in any dimension the same
ained, but they measure more or less than

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afforded us all the assistance in their power and the accommodation available in a period of continuous migration from room to room occasioned by the demolition of old laboratories and the erection of new ones, until finally the new buildings were taken over by the War Office. We also wish to express our thanks to the Royal Society for a grant of £30 towards the expenses of this work.

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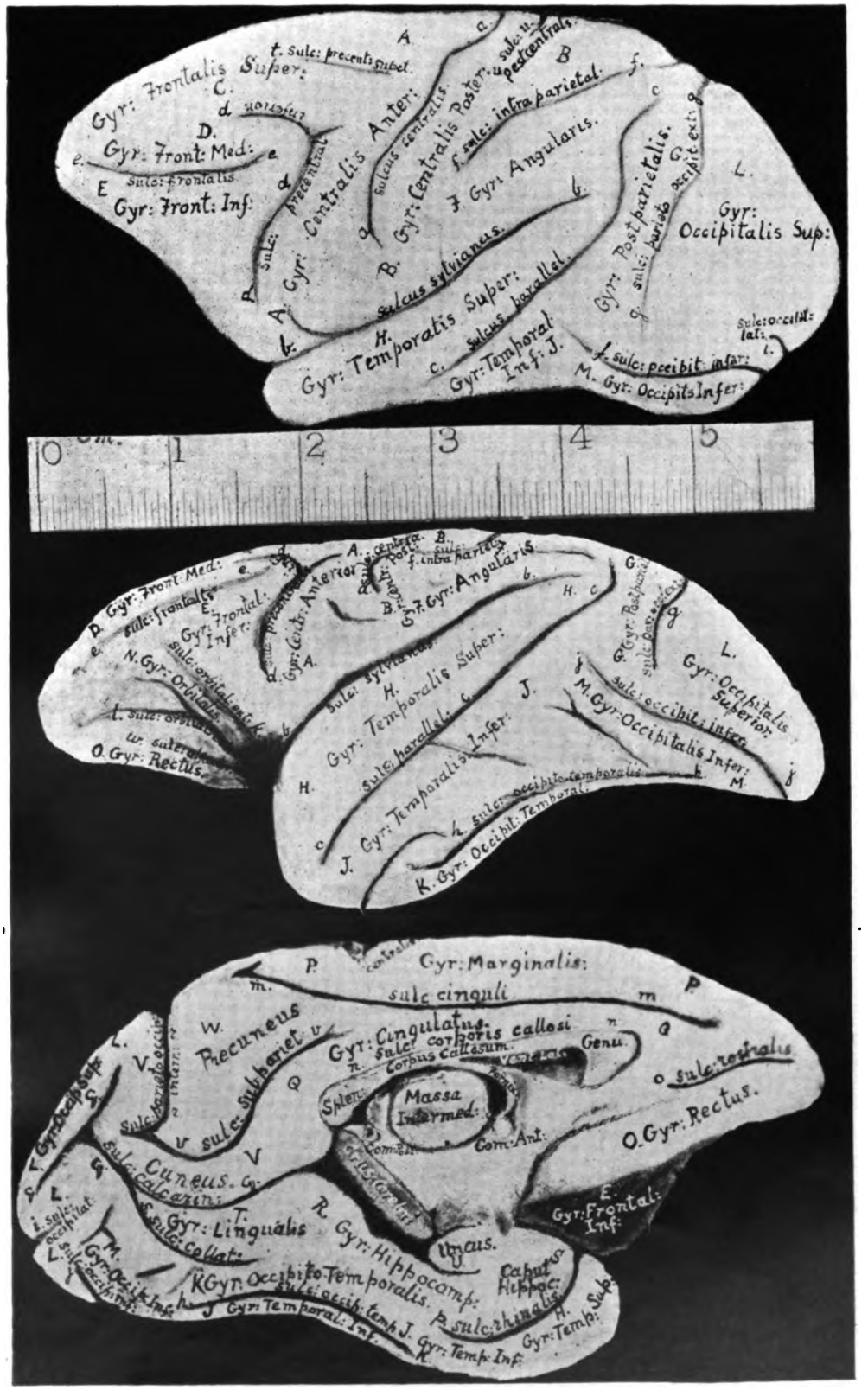

PLATE XL.—Brain of rhesus monkey. 1, lateral view, upper half: 2, lateral view, lower half; 3, lateral view, median sagittal section. (Enlarged 2 diameters.)

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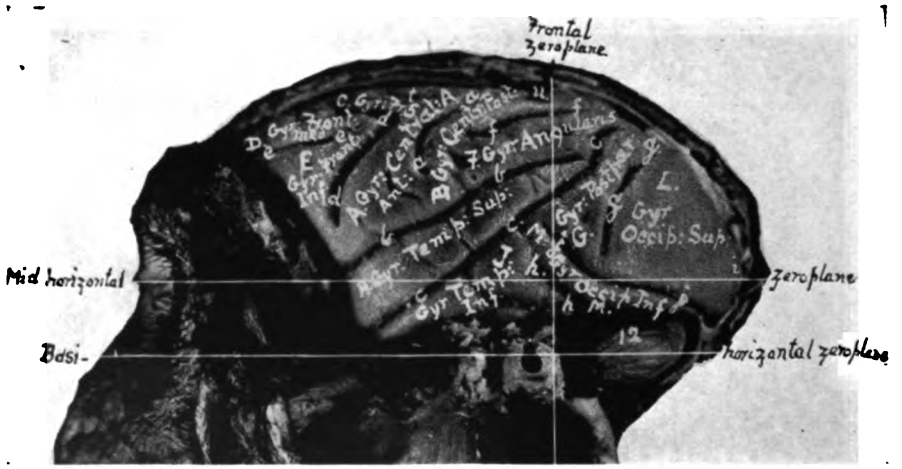
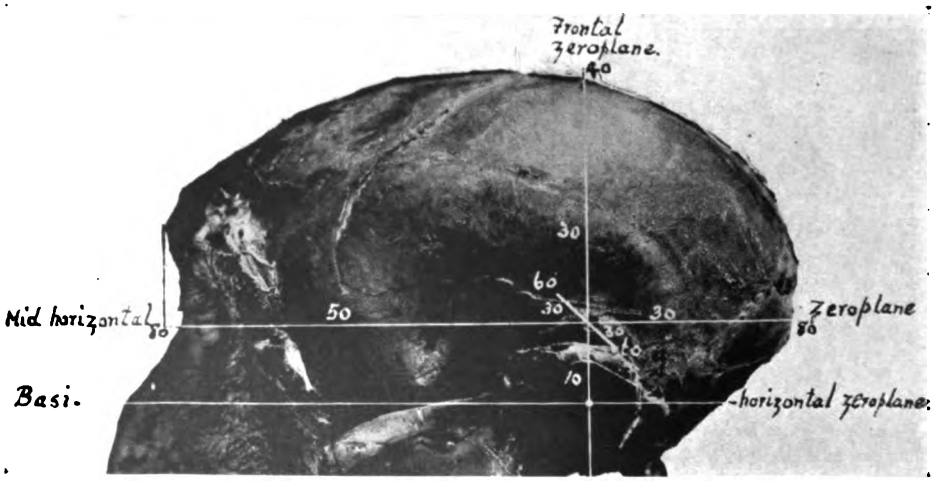
Median surface of right hemisphere.



Left hemisphere of brain, outer surface.



Surface of skull from left side.

XLI.—Projection of zero planes on cranium and brain of rhesus *in situ*. (Natural size. Dimensions of standard rhesus in millimeters.)

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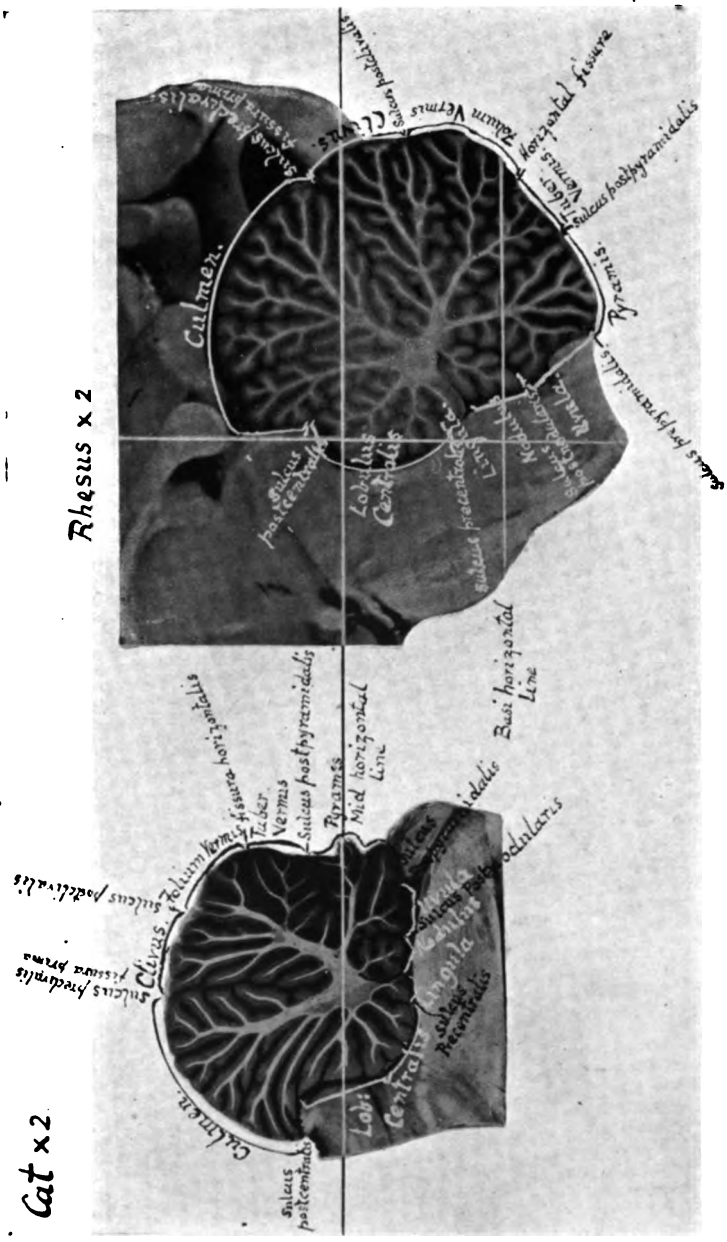

PLATE XLII.—Median sagittal section of vermis of cerebellum in rheesus monkey and cat, showing corresponding divisions and relations to horizontal zero planes in corresponding positions. (Enlarged 2 diameters.)

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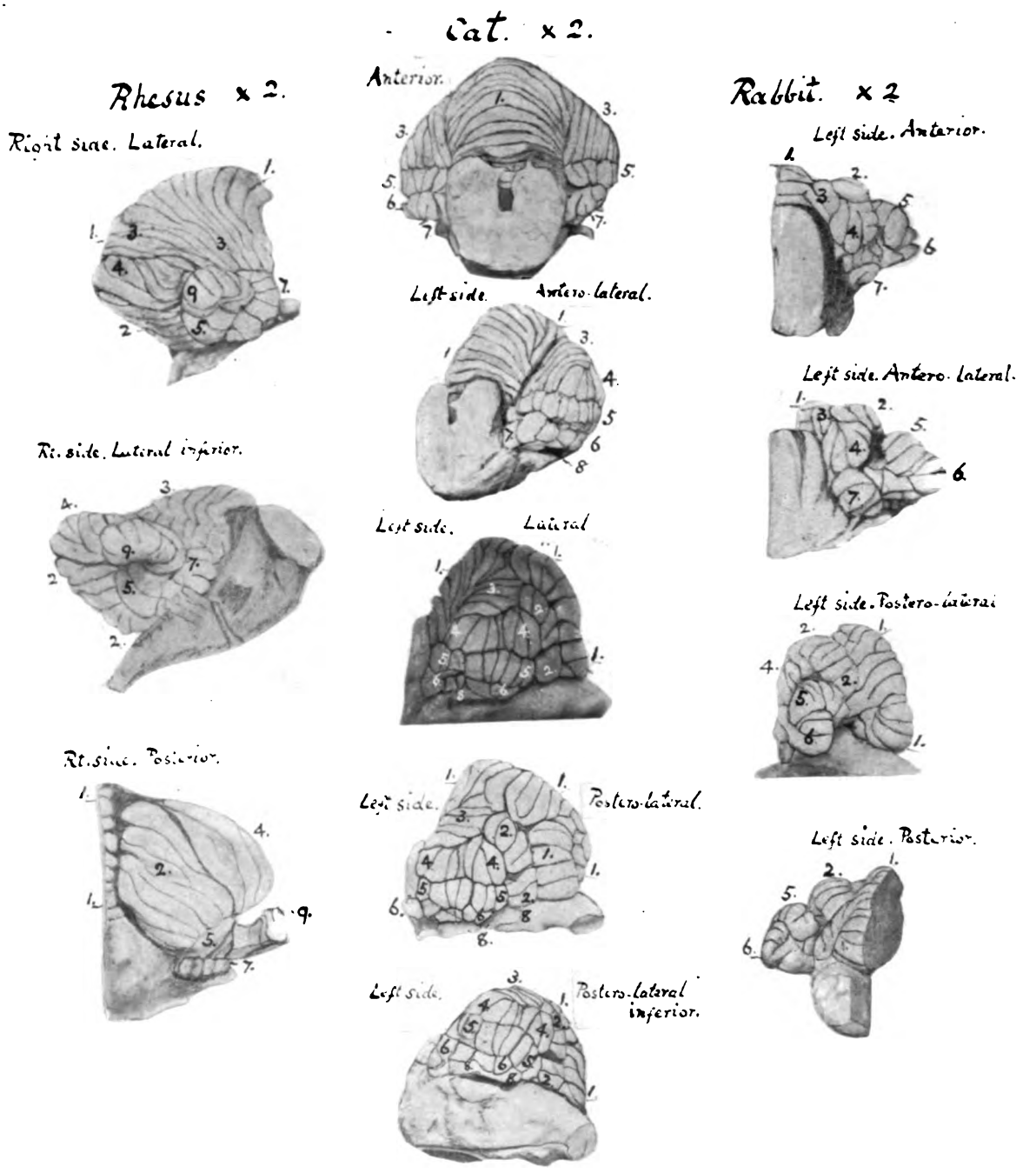

PLATE XLIII.—Illustrations of cerebellum of rhesus monkey, cat and rabbit, showing corresponding structures. (Enlarged 2 diameters.) 1, vermis; 2, paramesial lobule: 3, anterior pennate lobule; 4, posterior pennate lobule; 5, dorsal parafloccculus; 6, ventral parafloccculus; 7, flocculus; 8, peduncle of flocculus; 9, dorsal parafloccculus, lateral process. (Reduced ⅙.)

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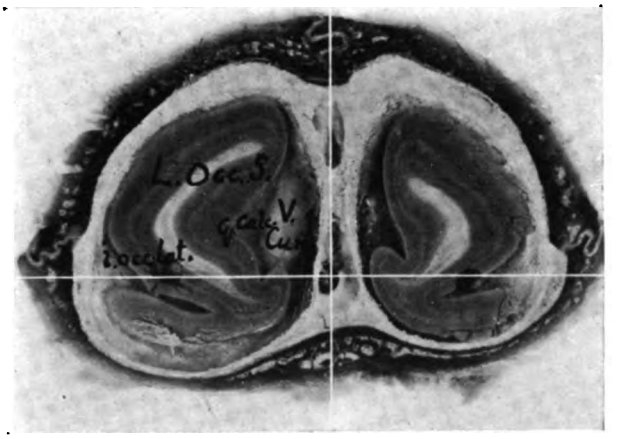
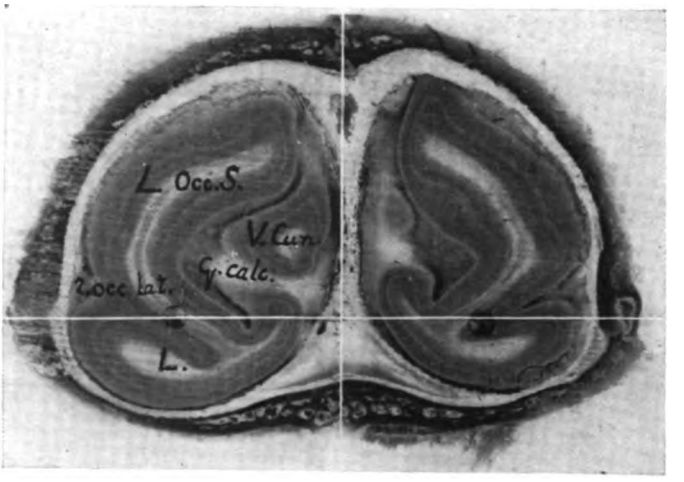


POSTERIOR FRONTAL LAMELLA. XXV.



POSTERIOR FRONTAL LAMELLA. XXIII.

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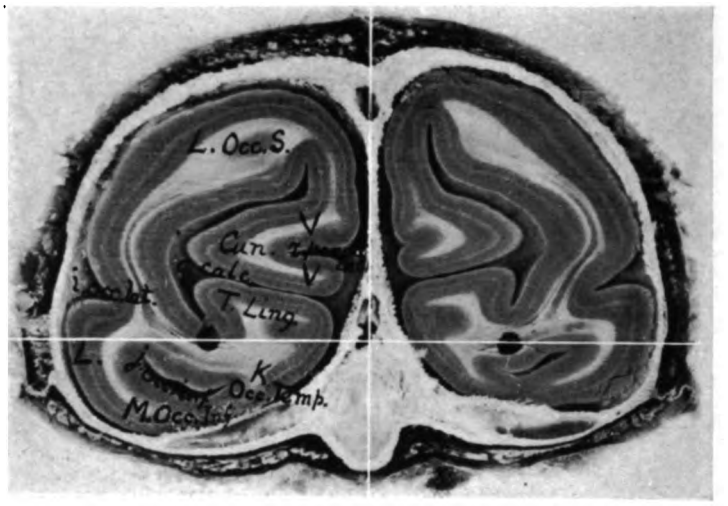
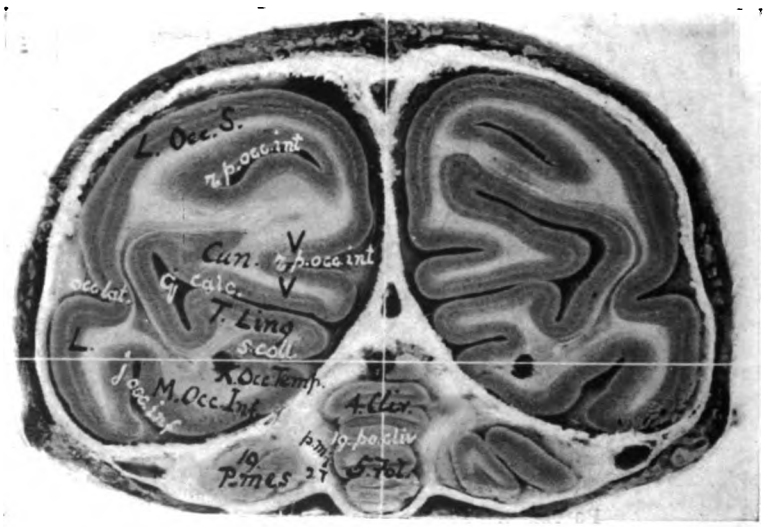


POSTERIOR FRONTAL LAMELLA. XXI.



POSTERIOR FRONTAL LAMELLA. XIX.

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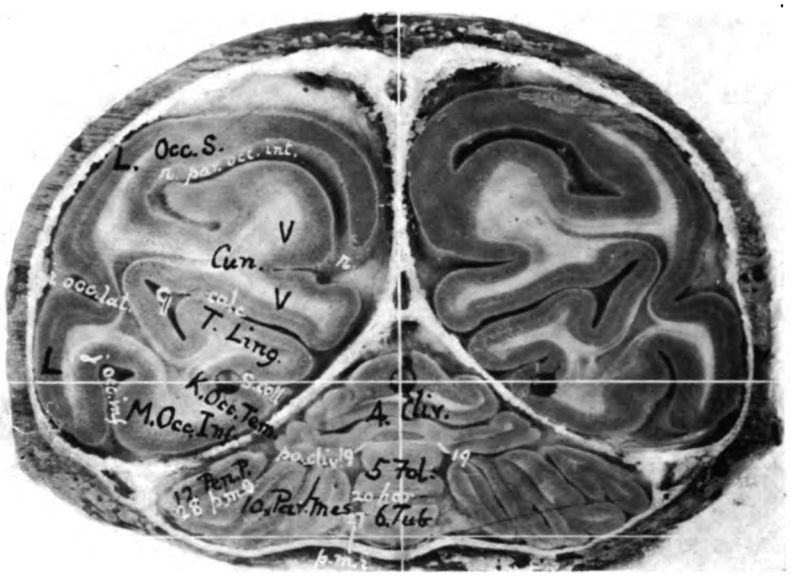
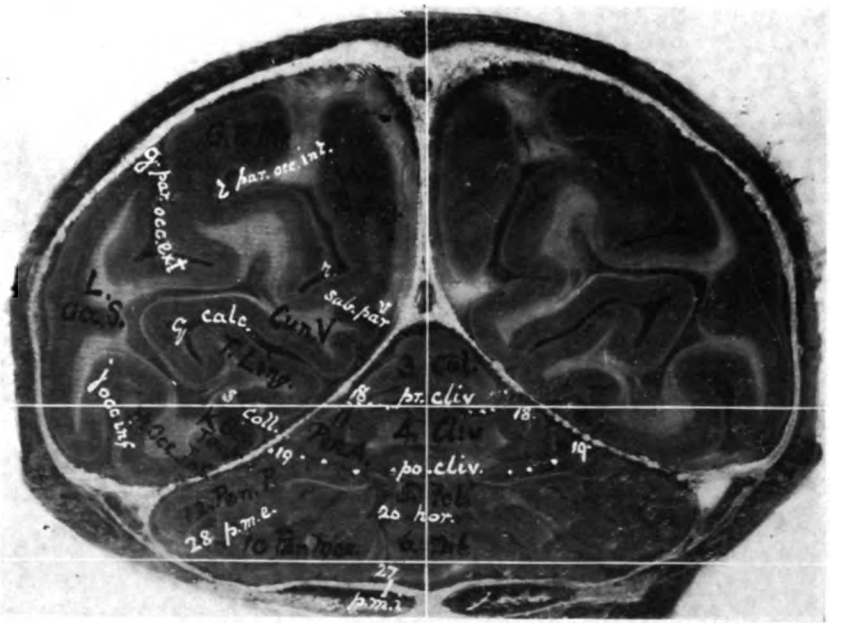


POSTERIOR FRONTAL LAMELLA. XVII.



POSTERIOR FRONTAL LAMELLA. XV.

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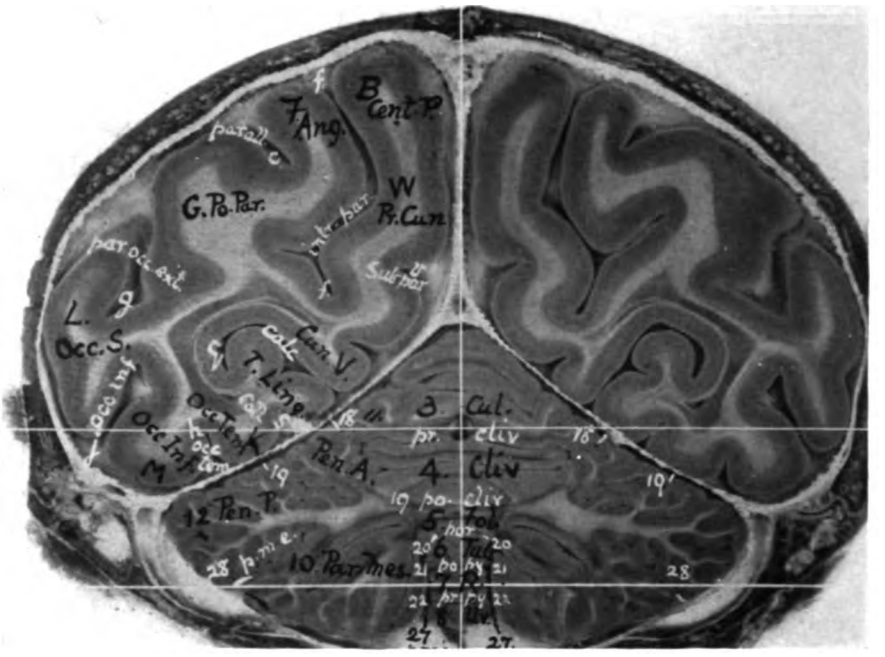
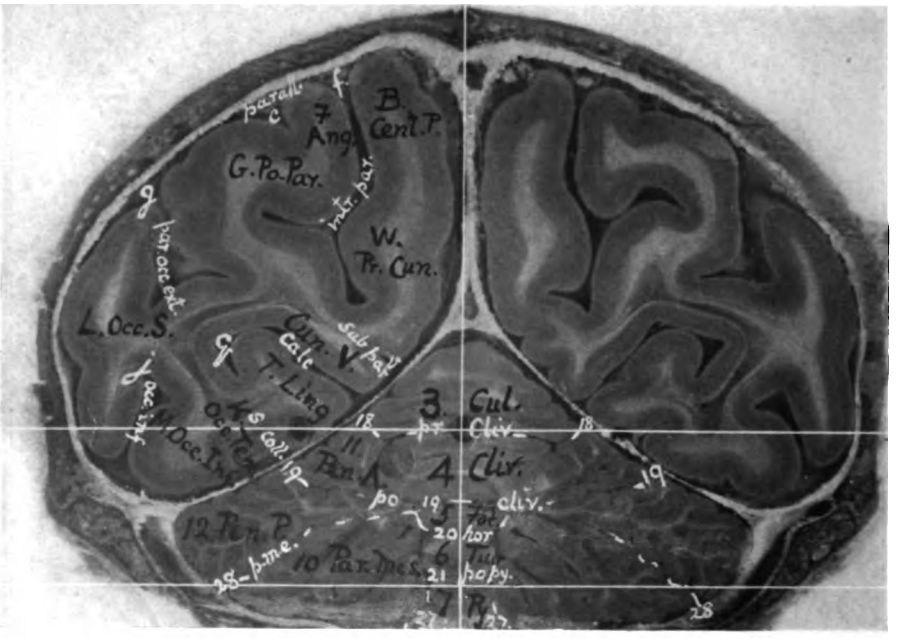


Posterior Frontal Lamella. XIII.



Posterior Frontal Lamella. XI.

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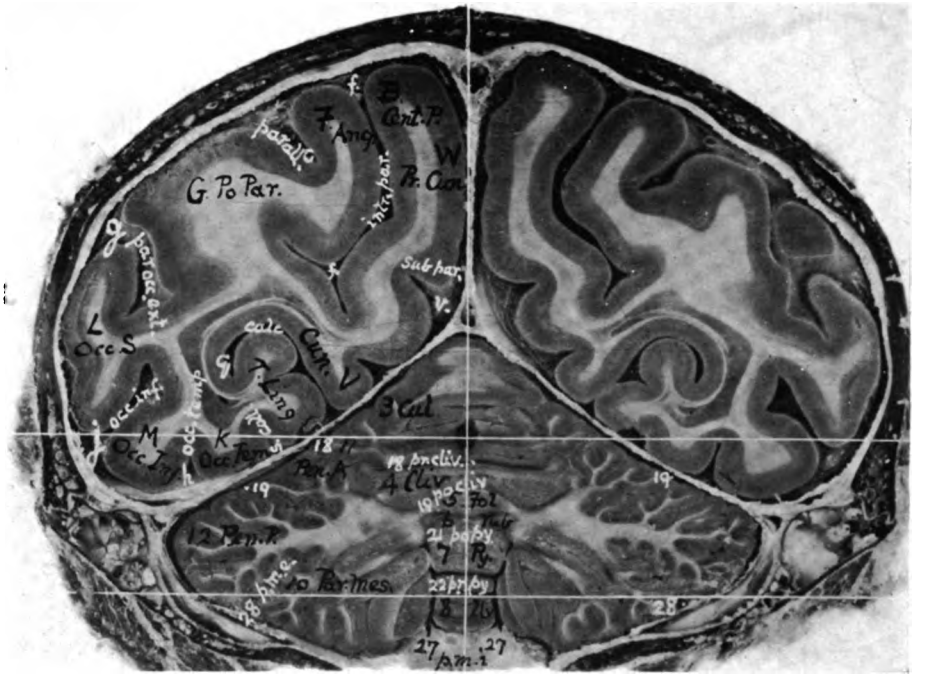
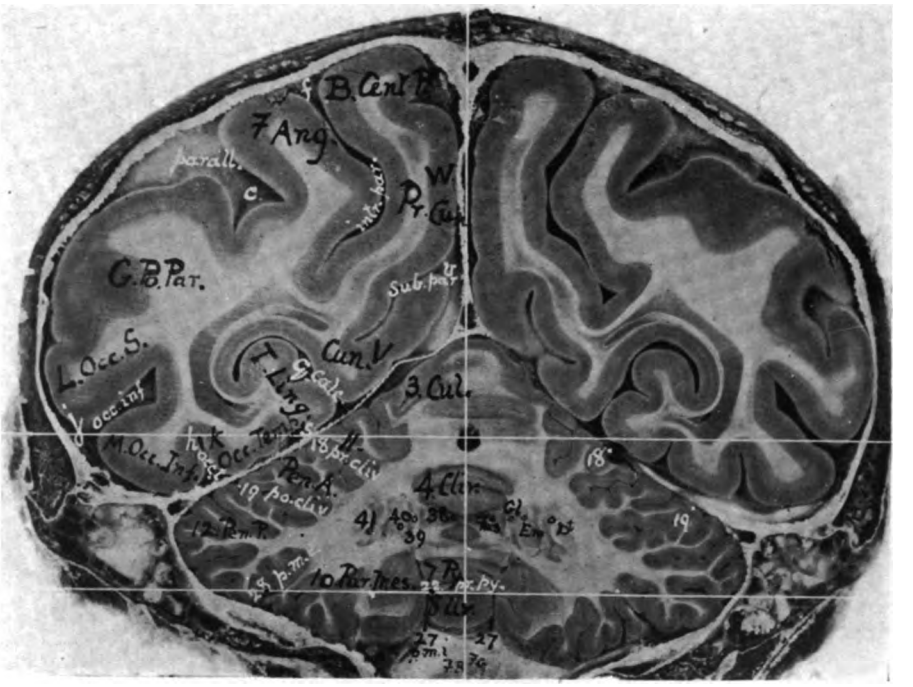


Posterior Frontal Lamella. X.



Posterior Frontal Lamella. IX.

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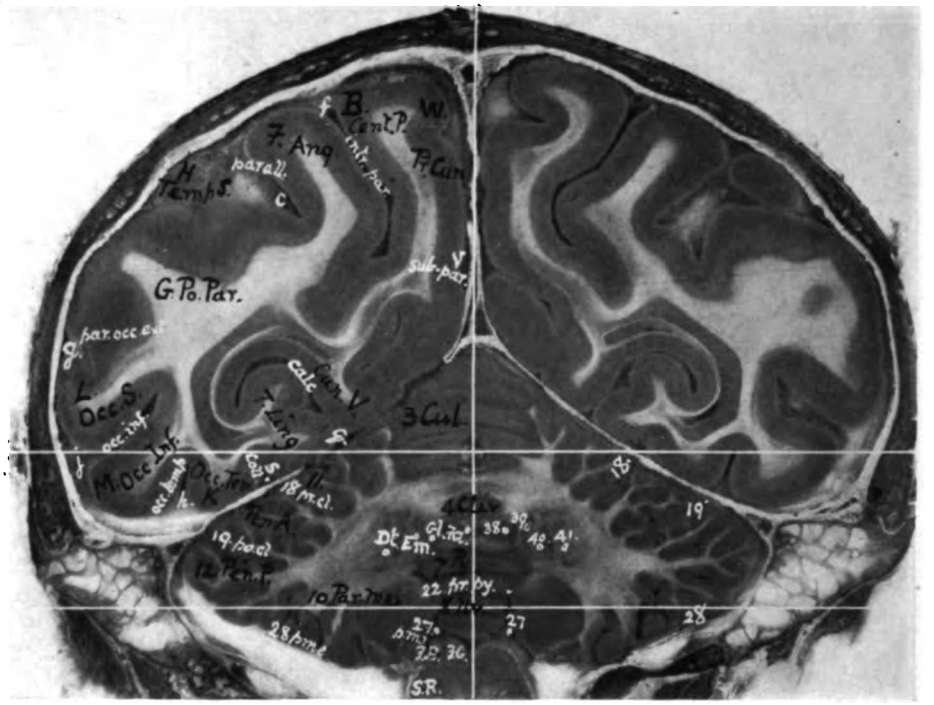
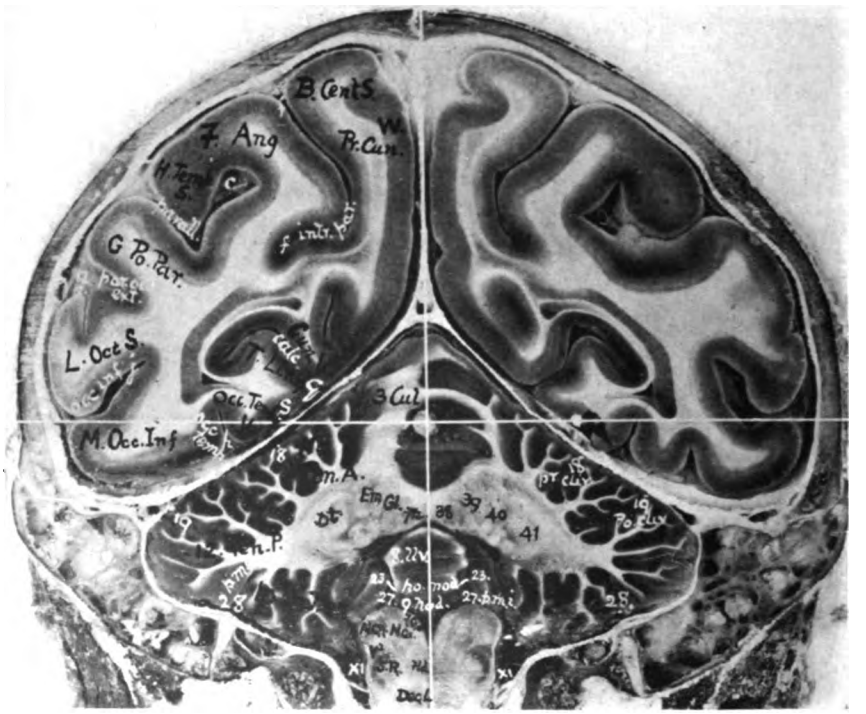


Posterior Frontal Lamella. VIII.



Posterior Frontal Lamella. VII.

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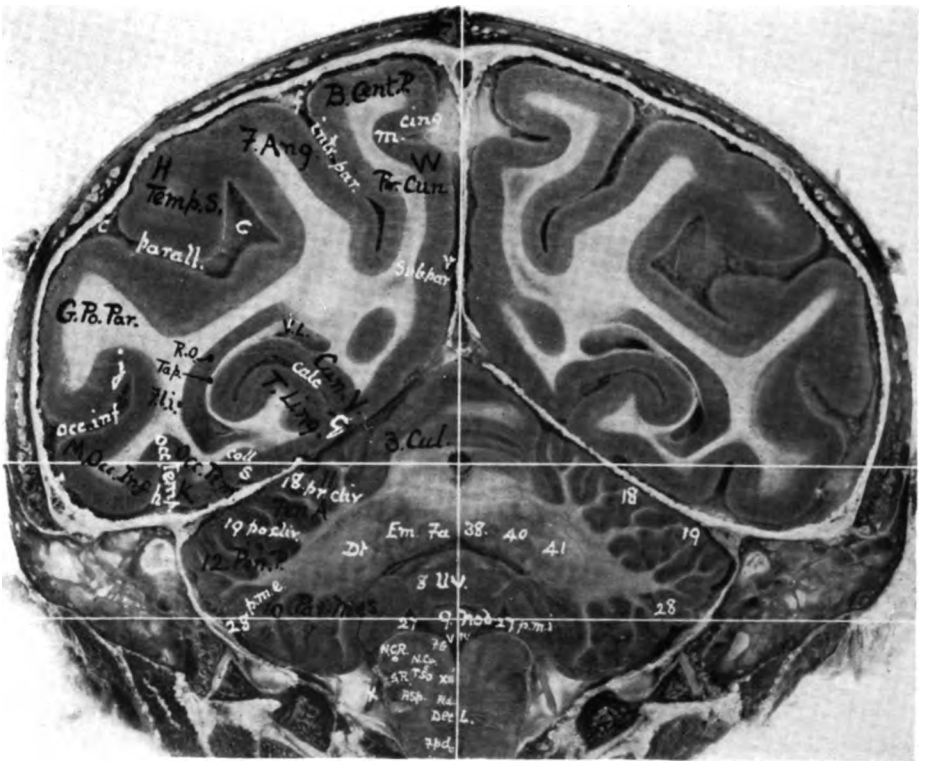
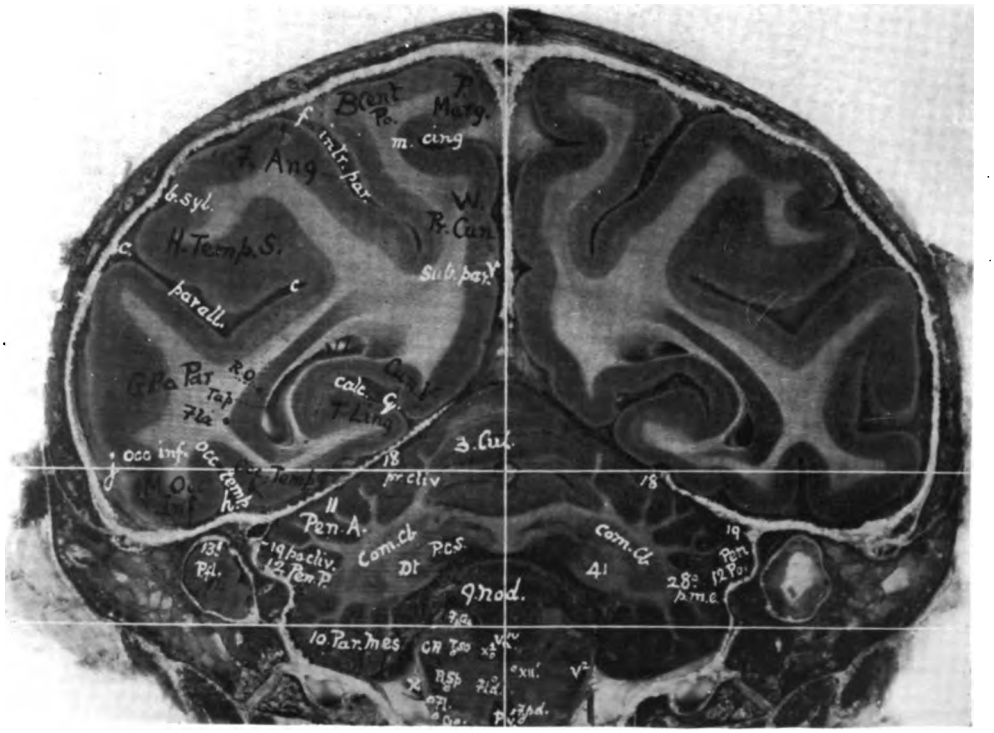


POSTERIOR FRONTAL LAMELLA. VI.



POSTERIOR FRONTAL LAMELLA. V.

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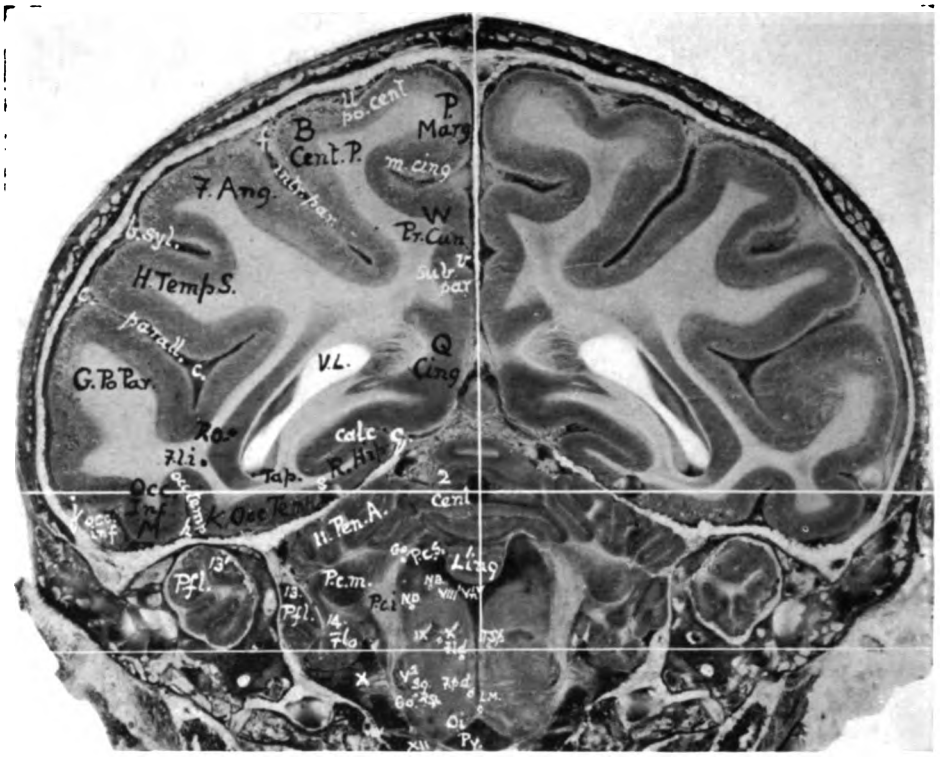
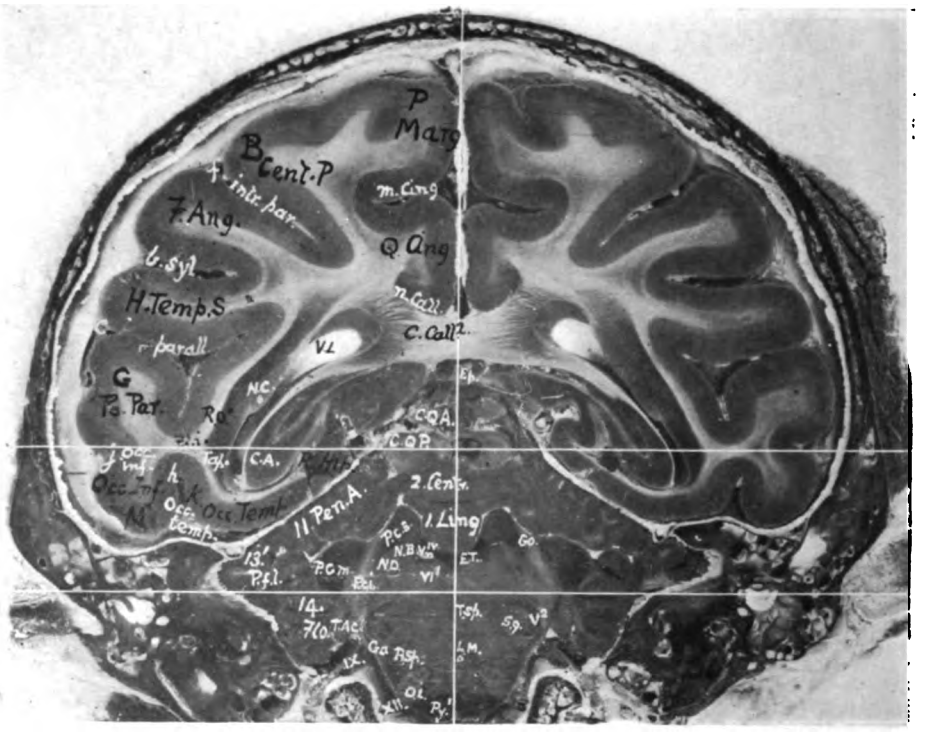


Posterior Frontal Lamella. IV.



Posterior Frontal Lamella. III.

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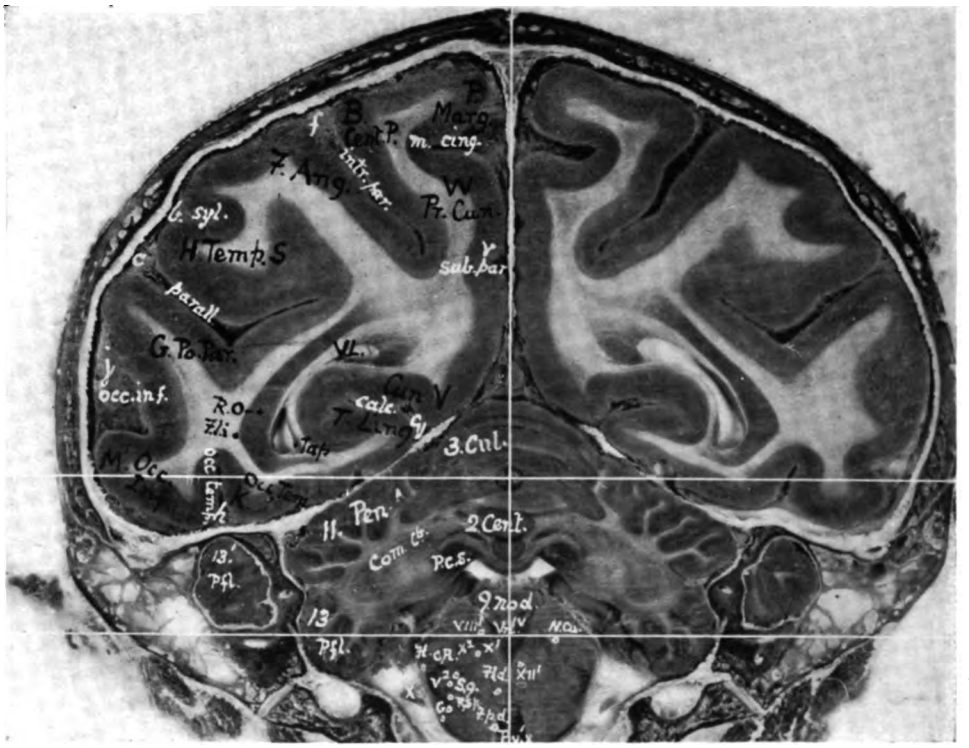
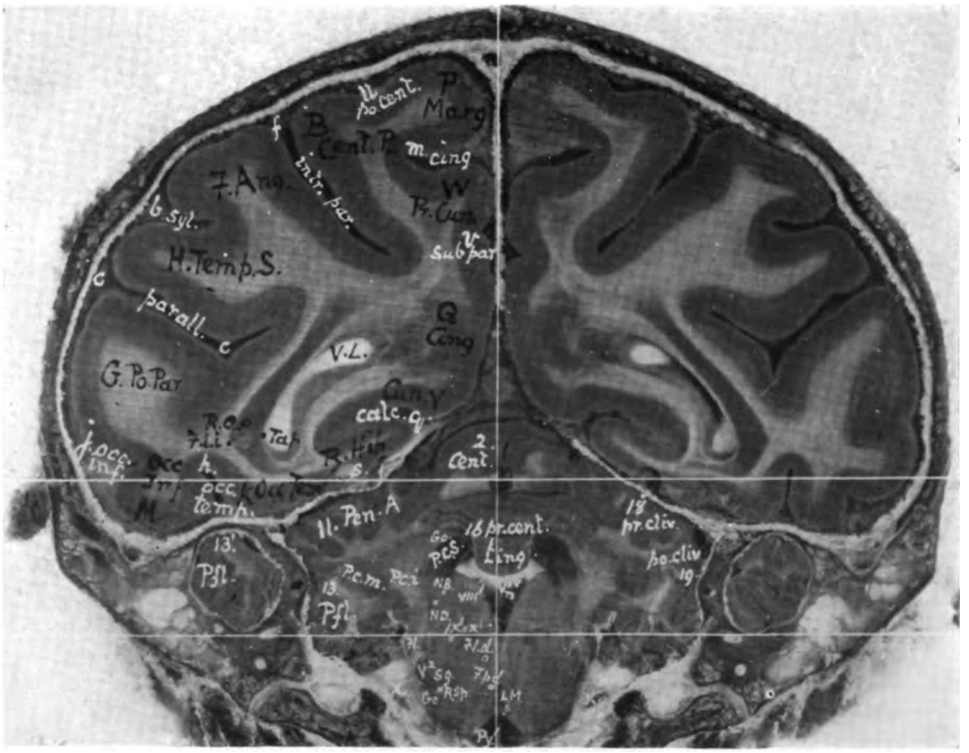


POSTERIOR FRONTAL LAMELLA. II.



POSTERIOR FRONTAL LAMELLA. I.

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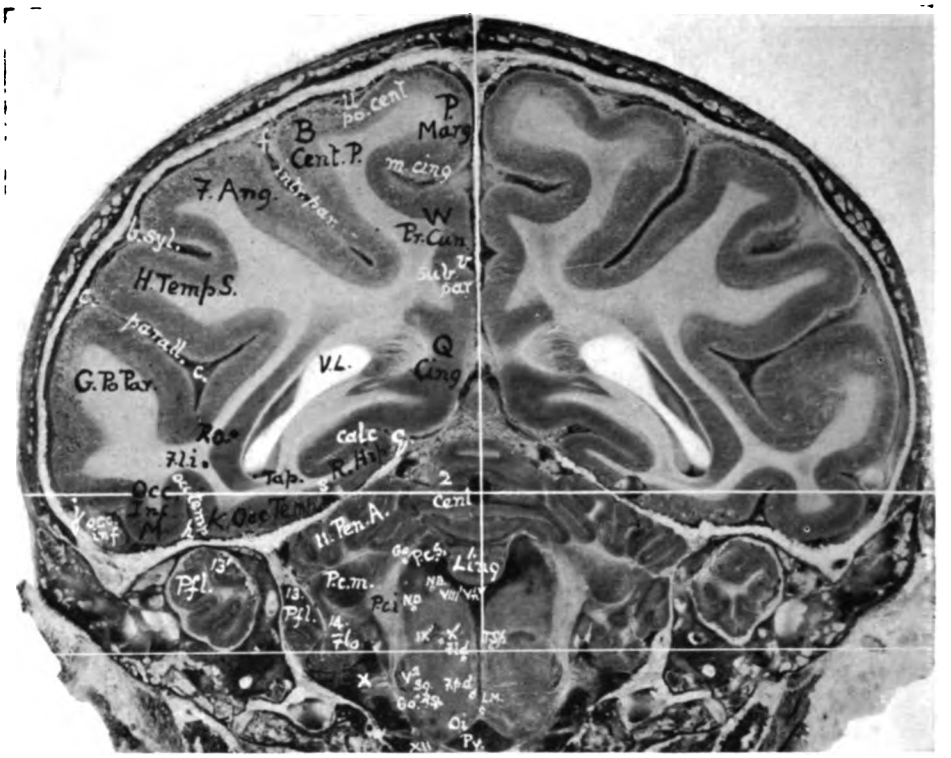
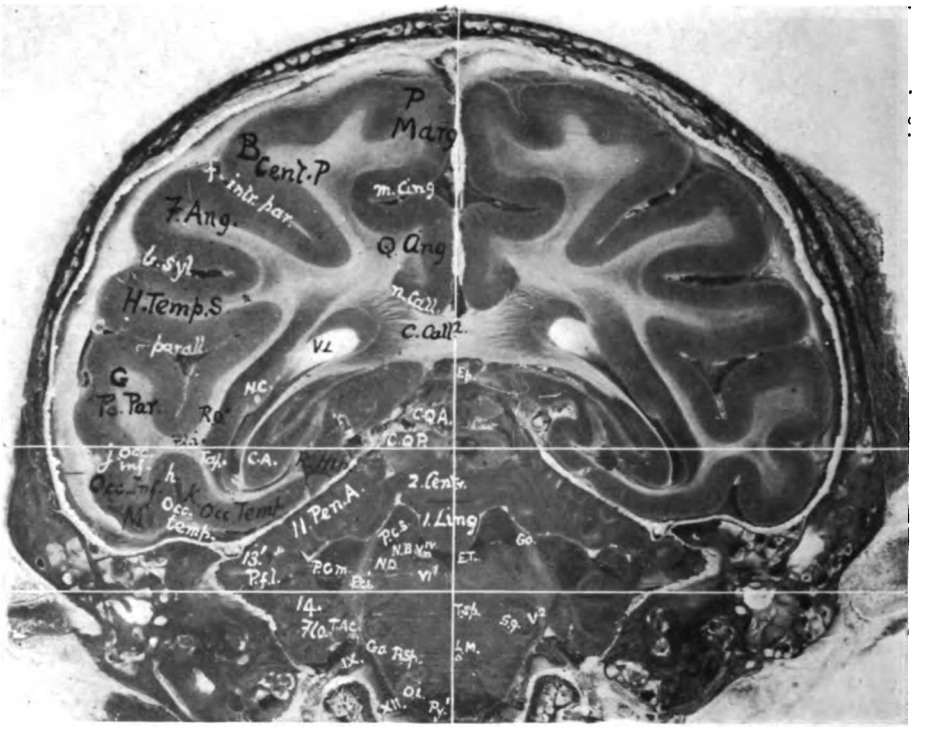


POSTERIOR FRONTAL LAMELLA. IV.



POSTERIOR FRONTAL LAMELLA. III.

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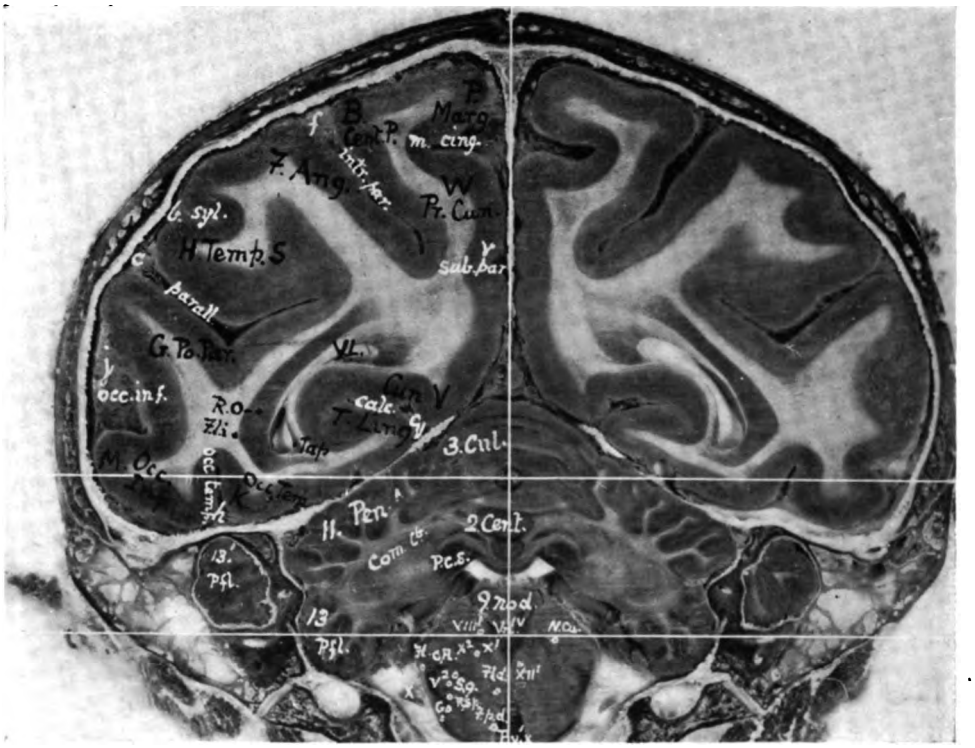
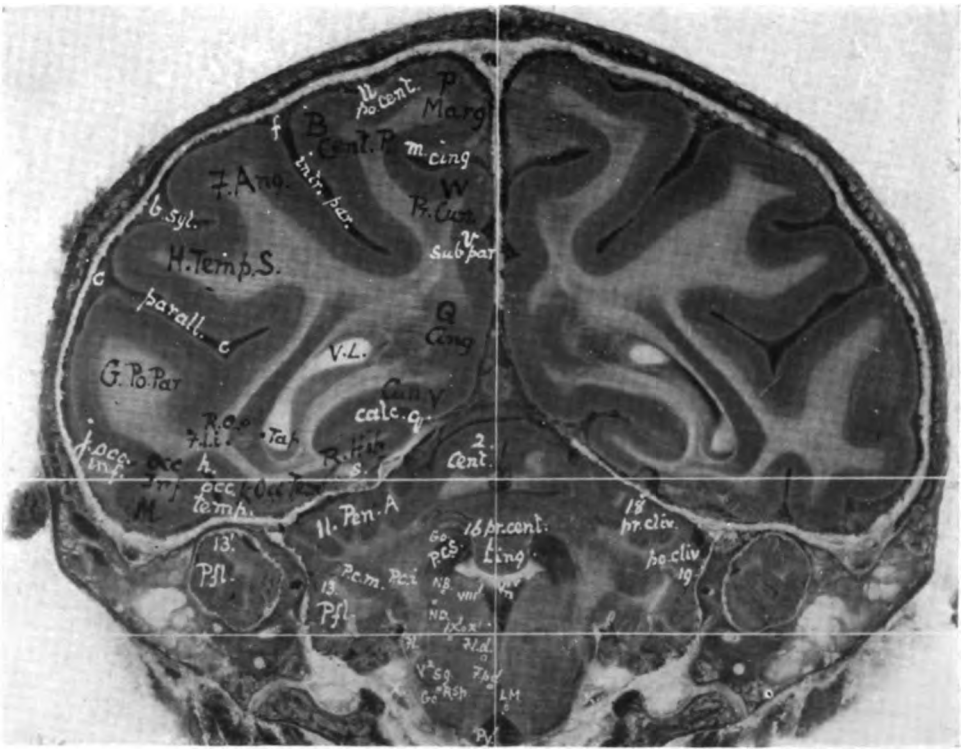


Posterior Frontal Lamella. II.



Posterior Frontal Lamella. I.

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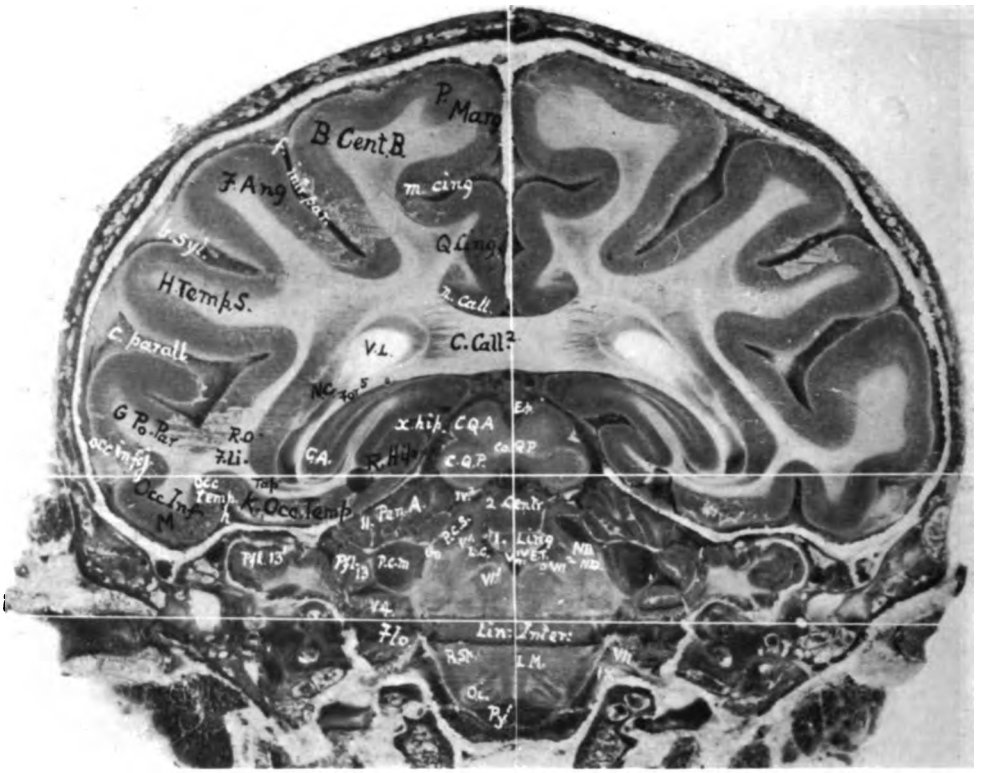
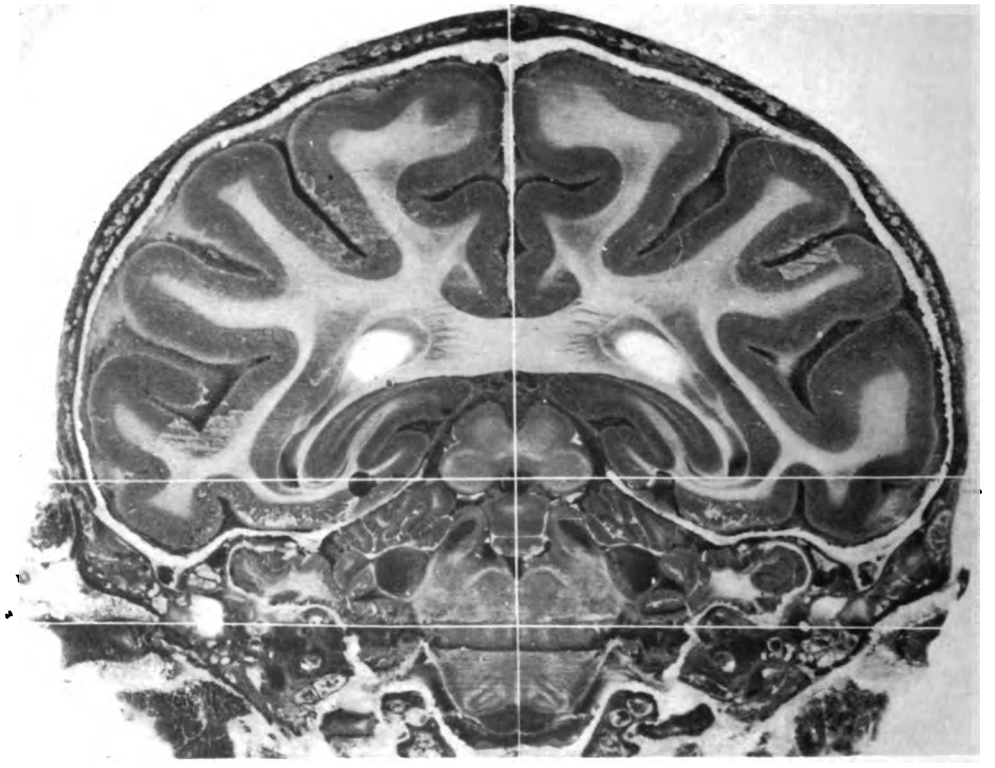


ANTERIOR FRONTAL LAMELLA. I.



ANTERIOR FRONTAL LAMELLA. I.

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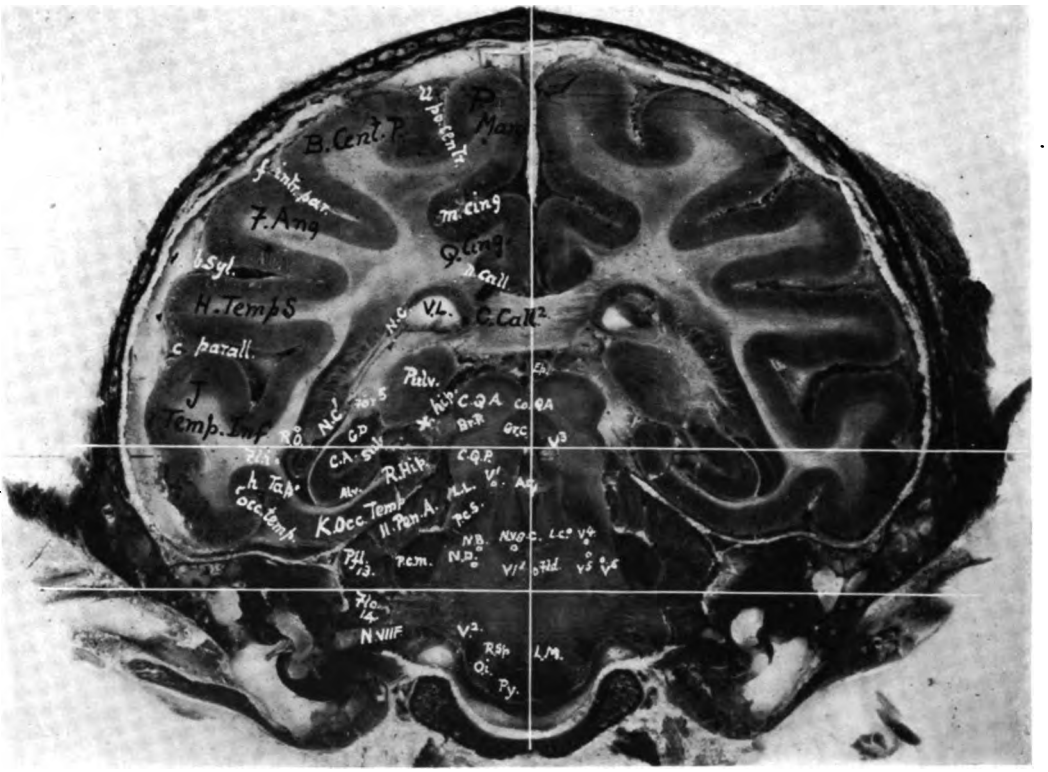

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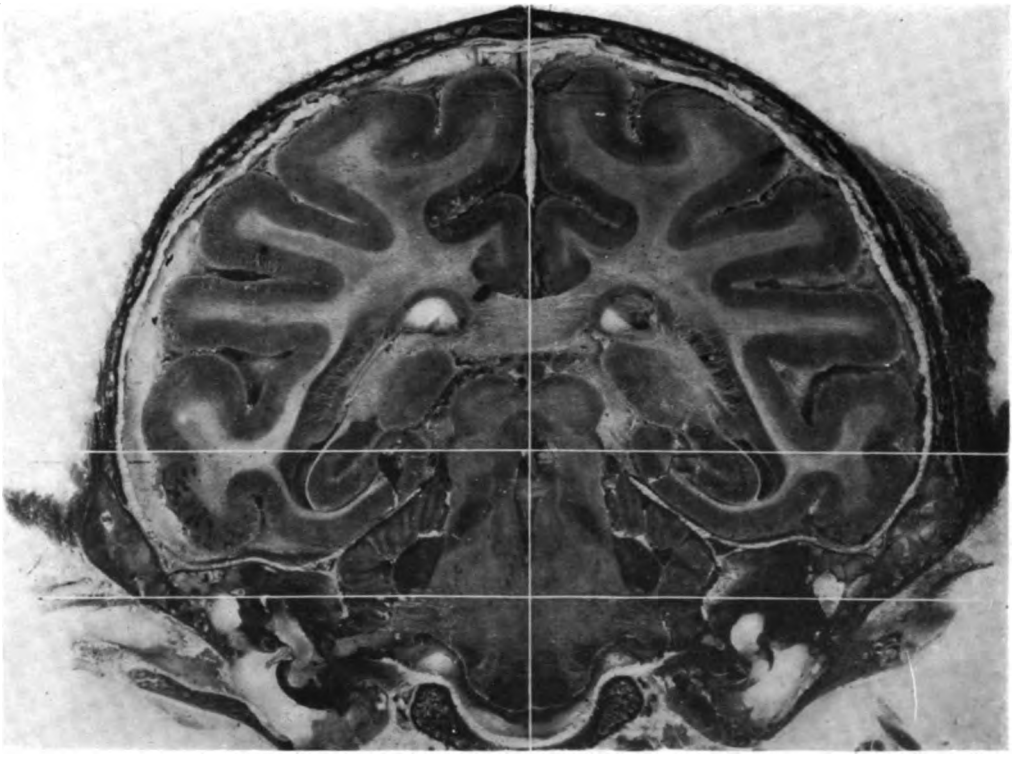

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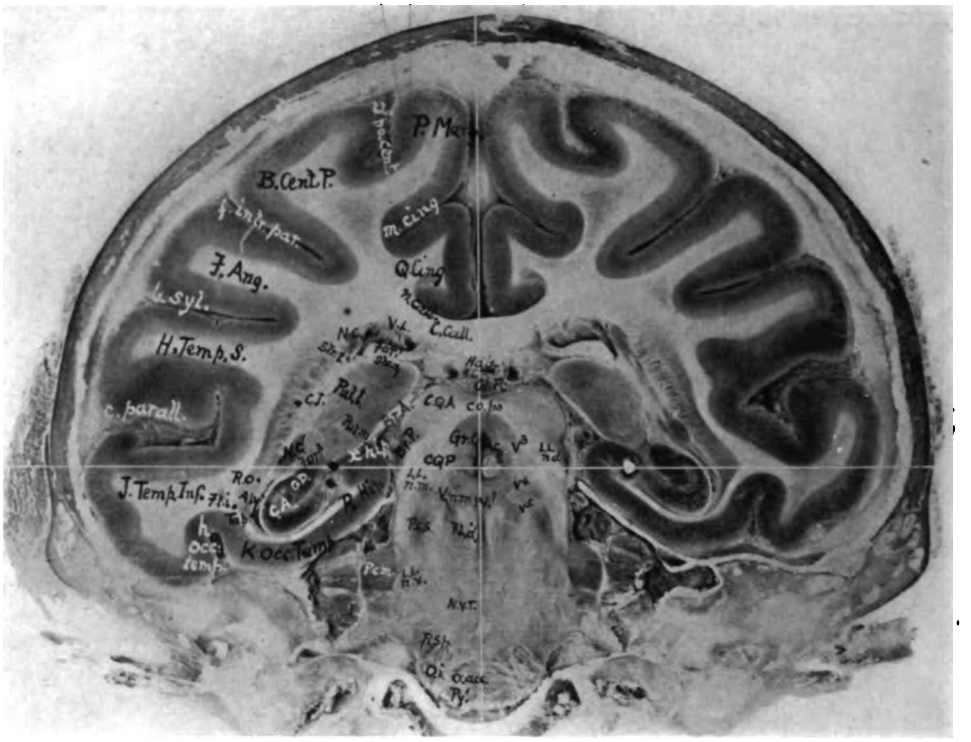

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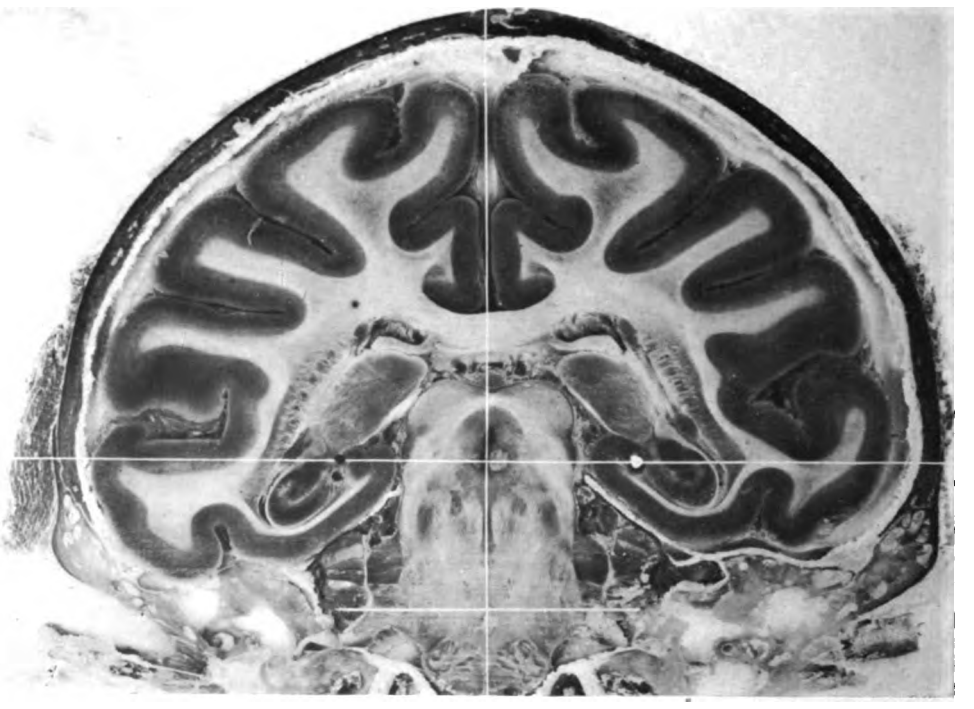

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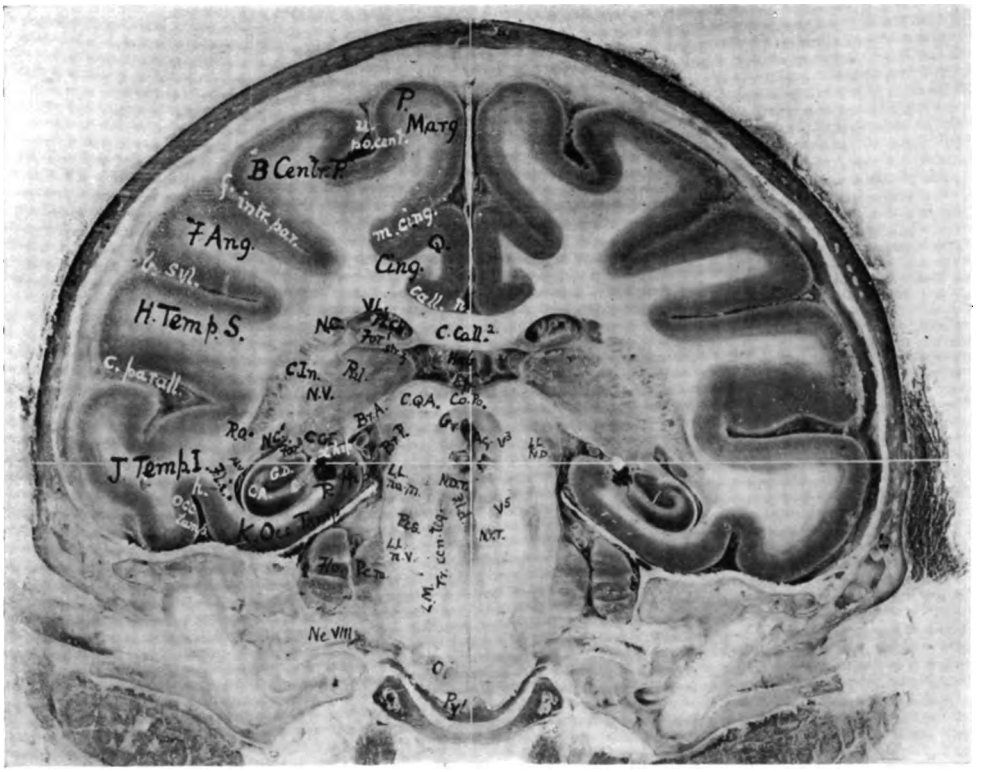

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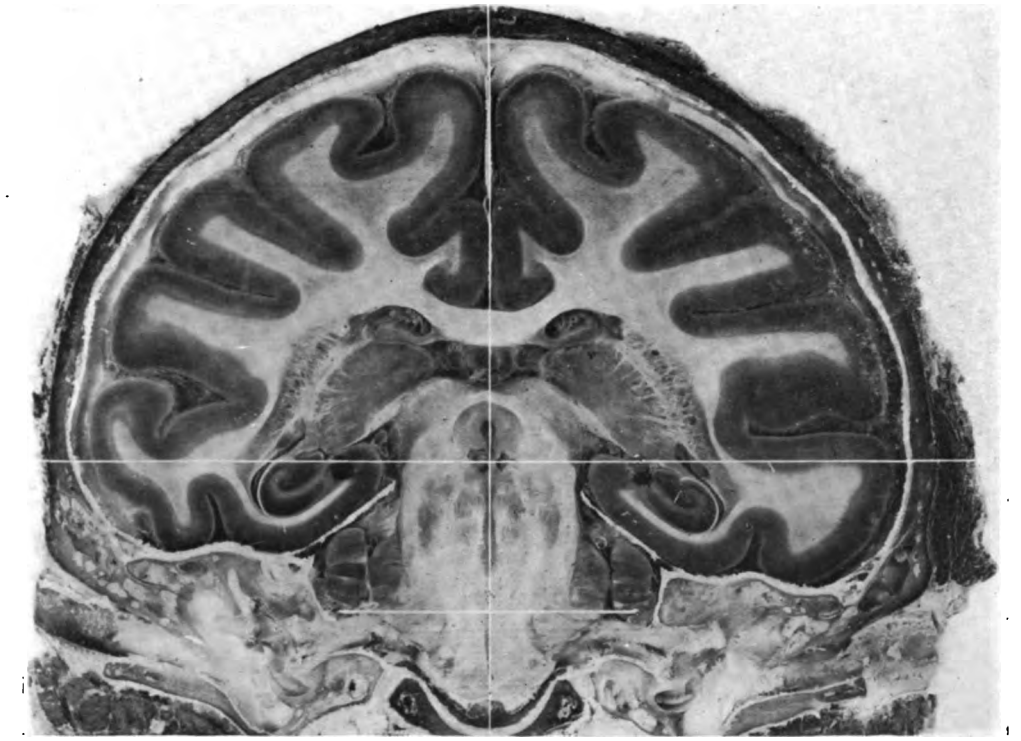

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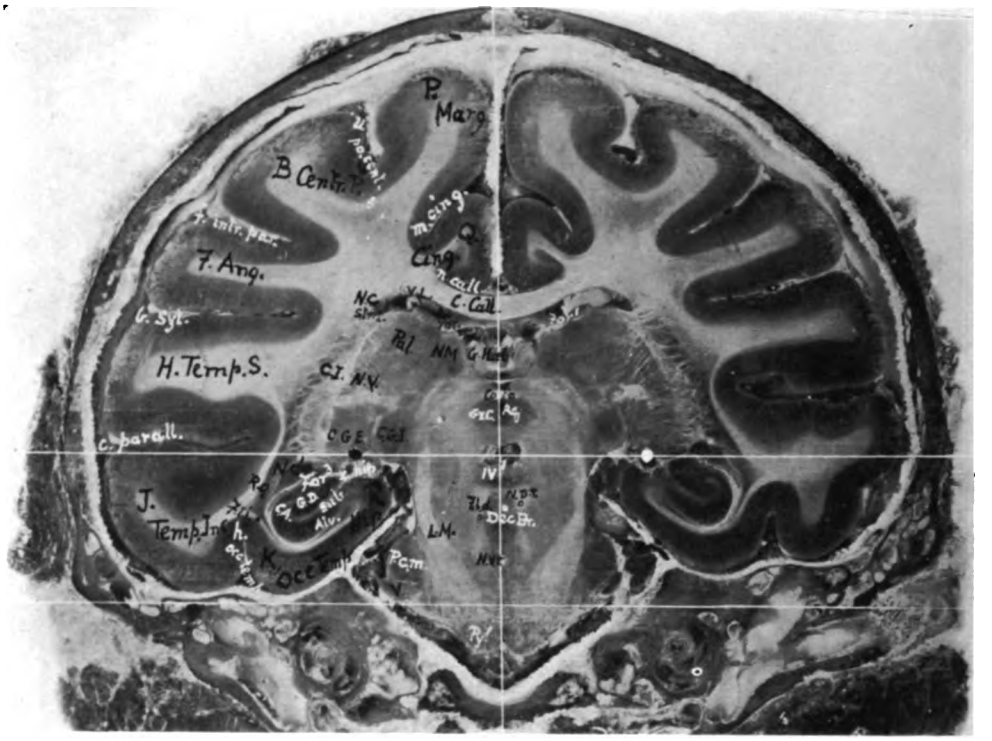

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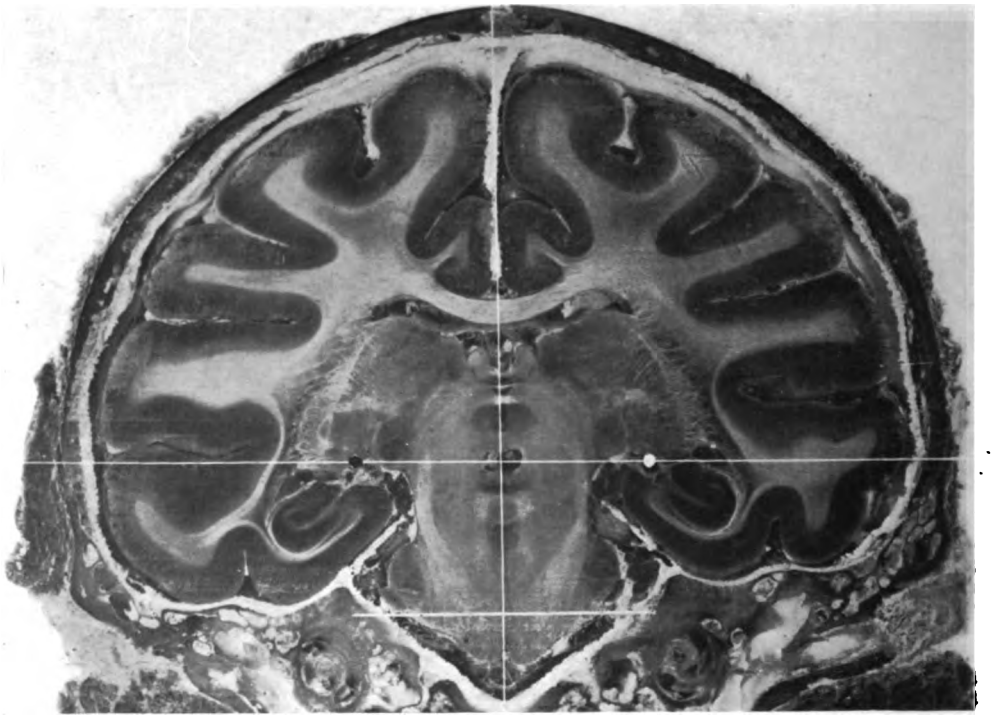

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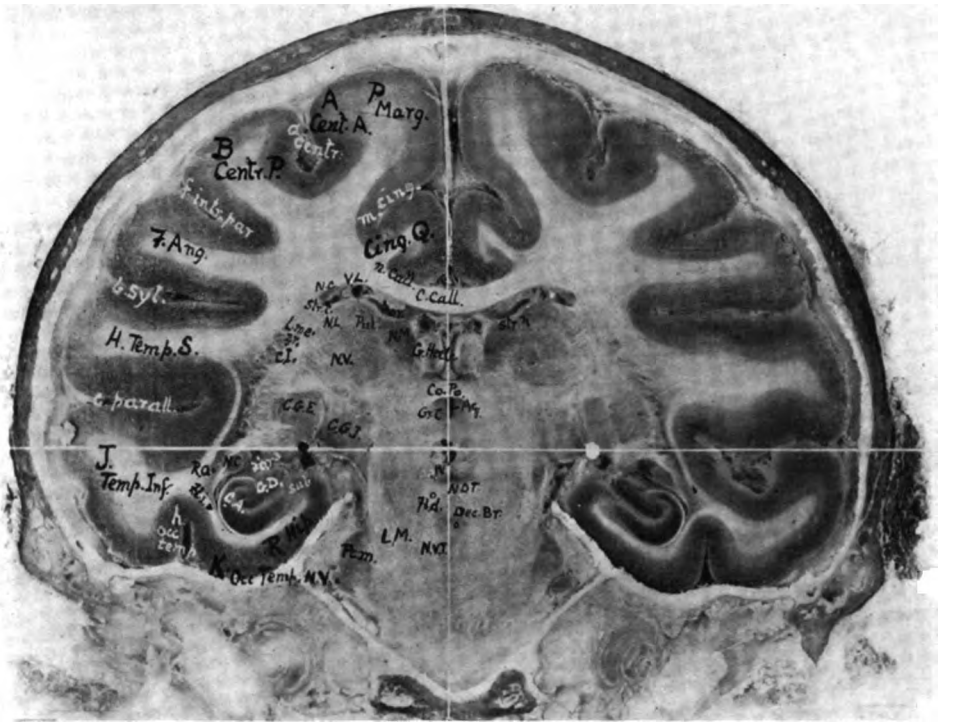

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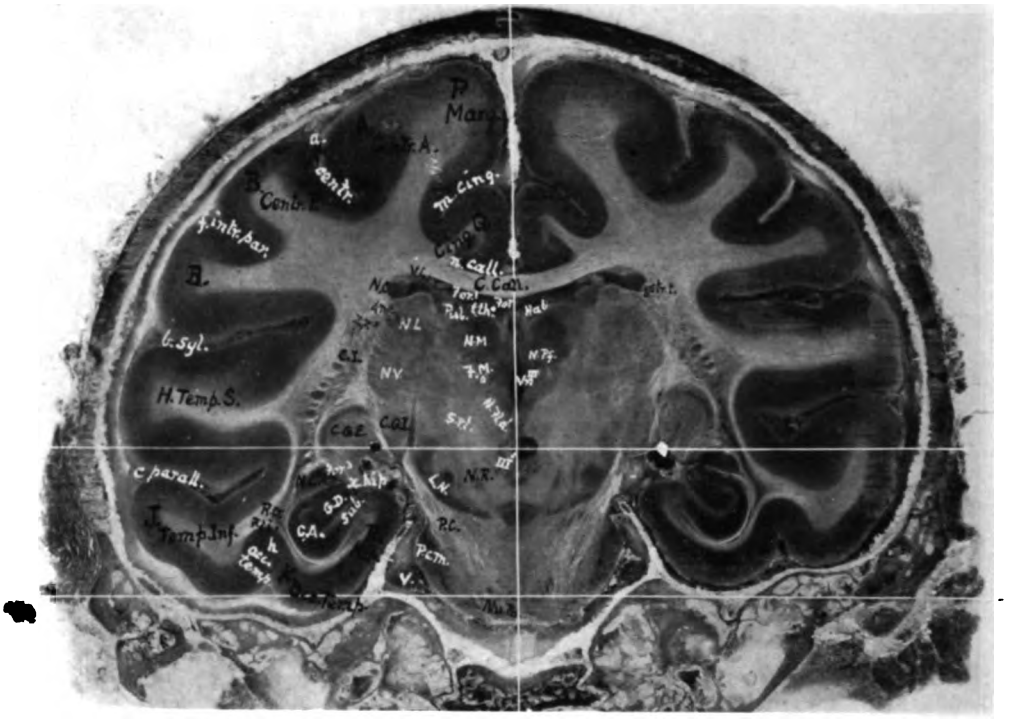

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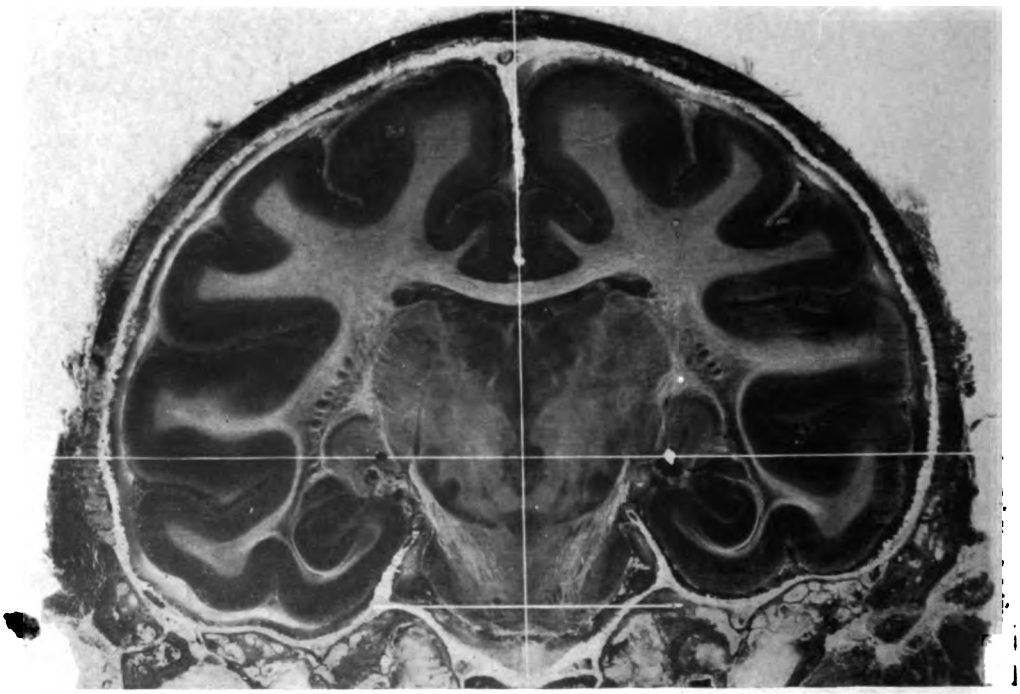

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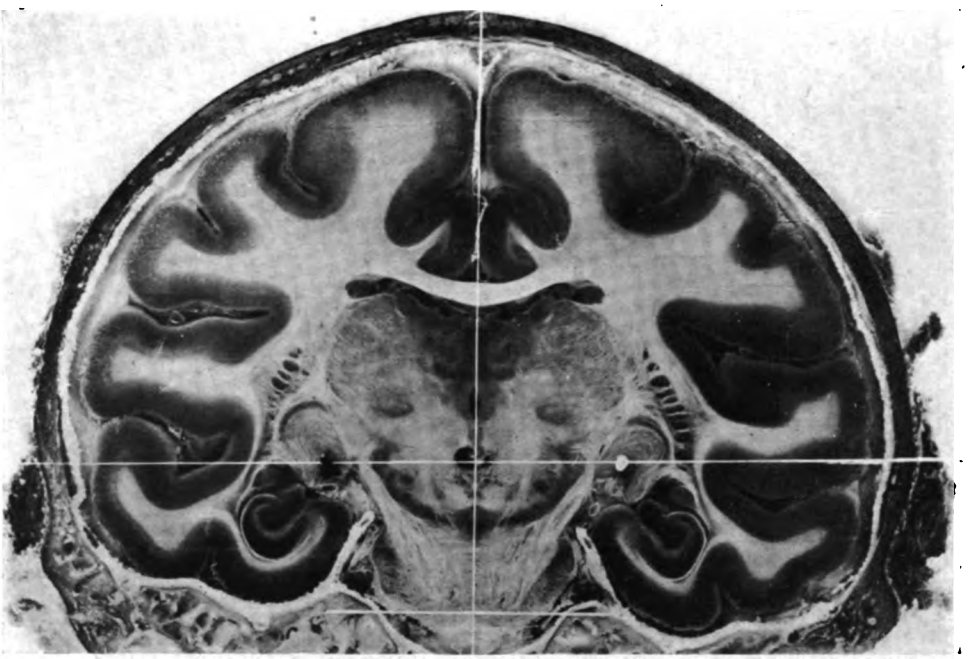

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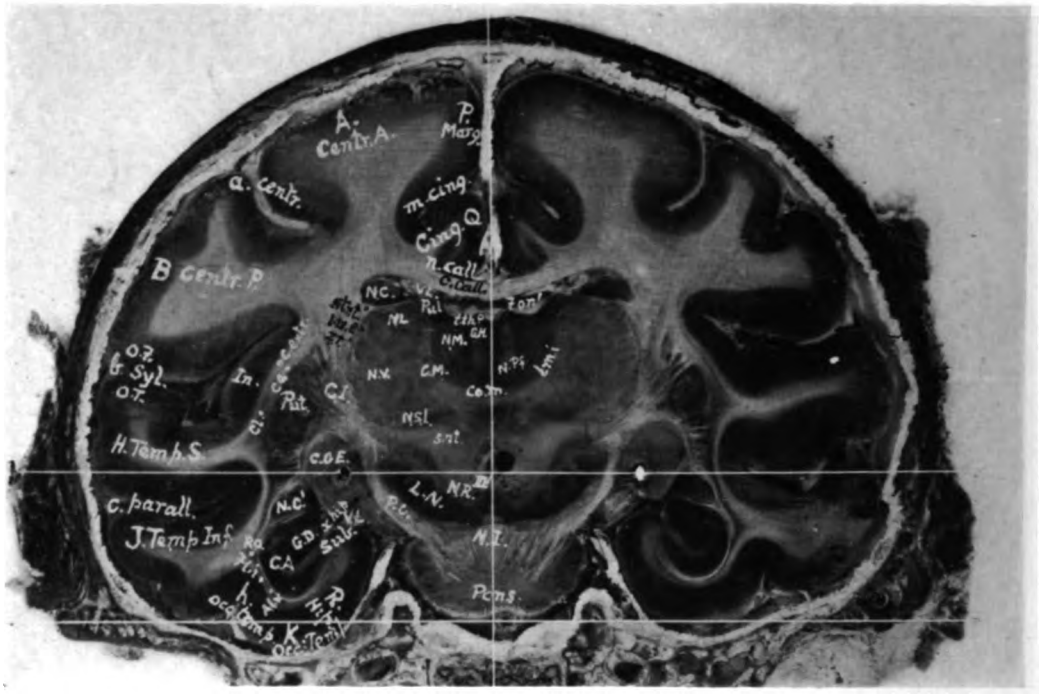

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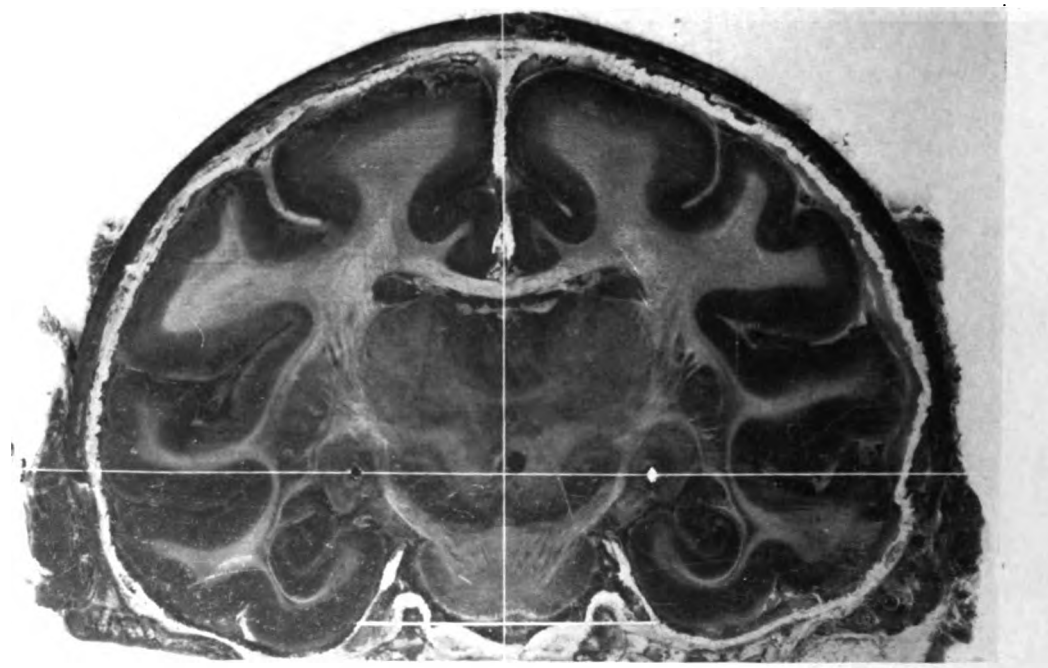

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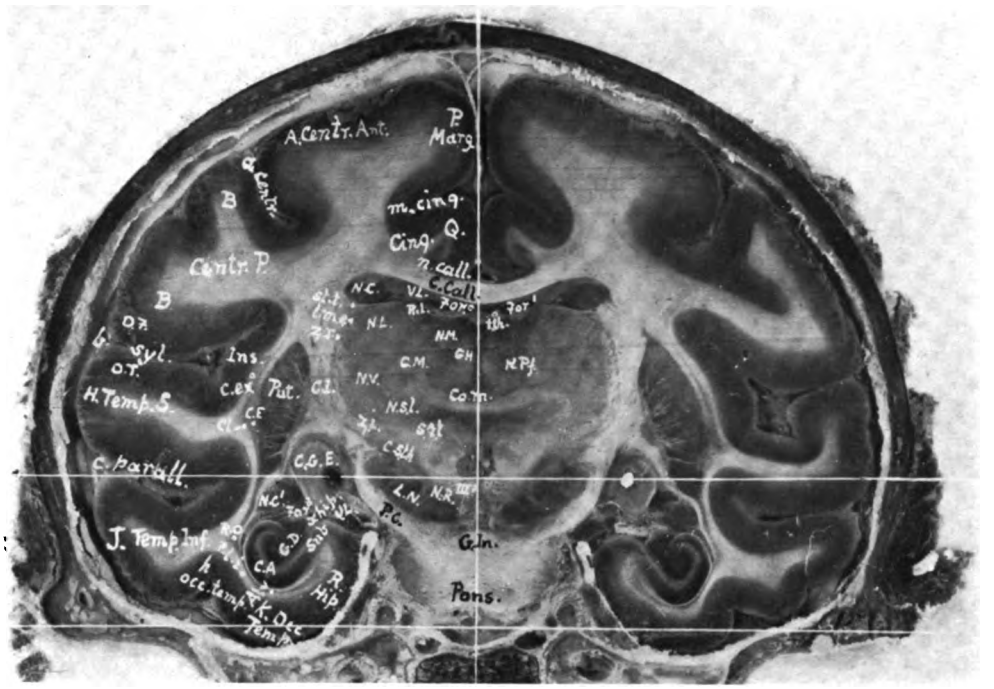

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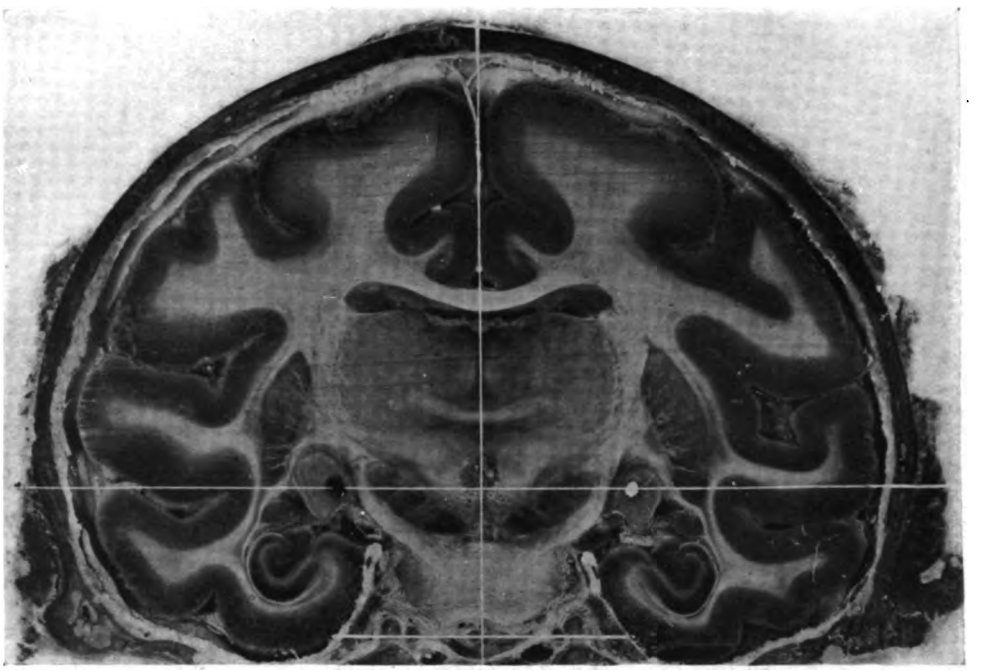

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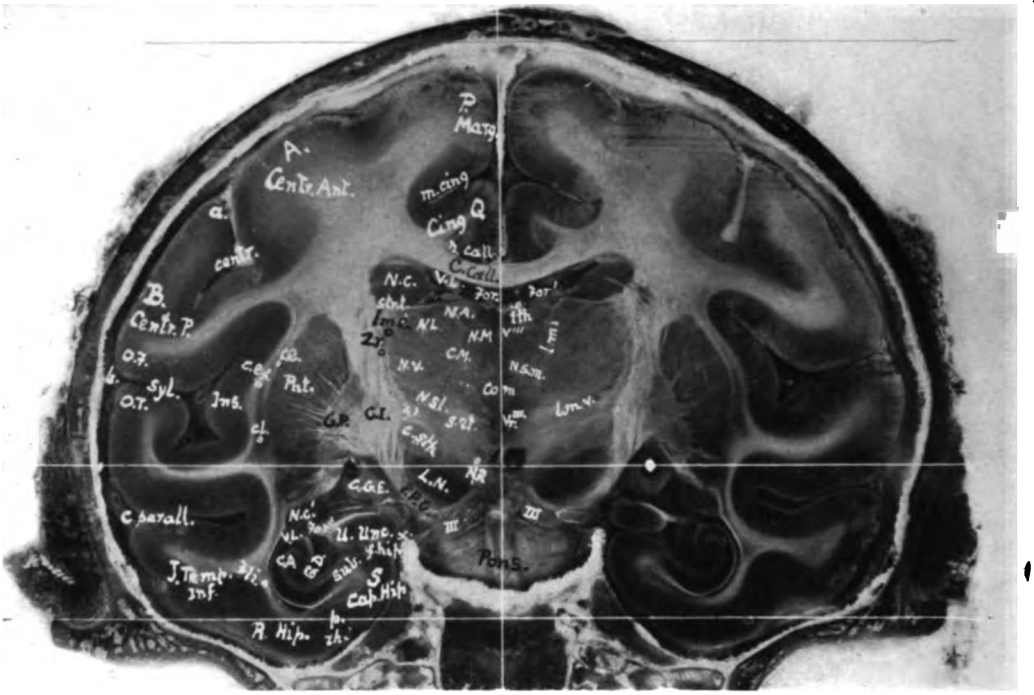

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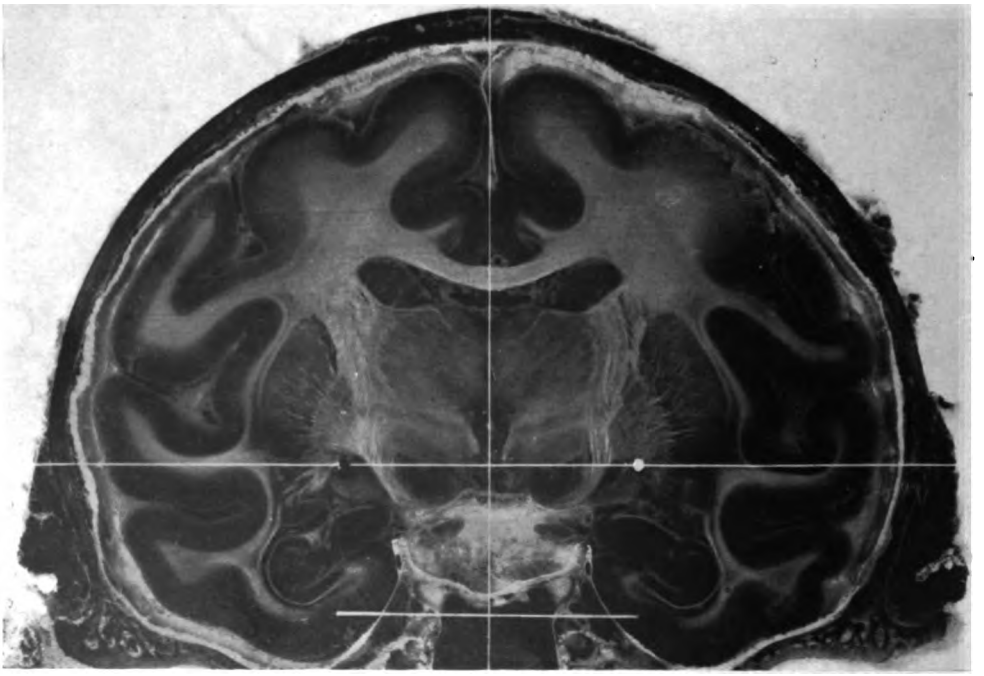

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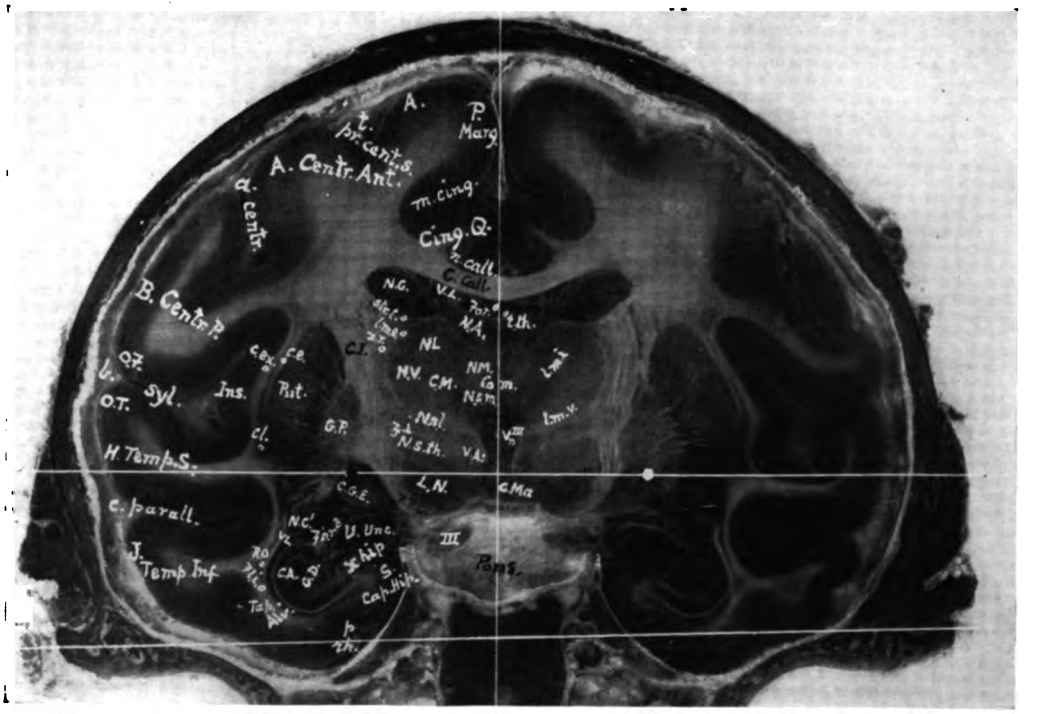

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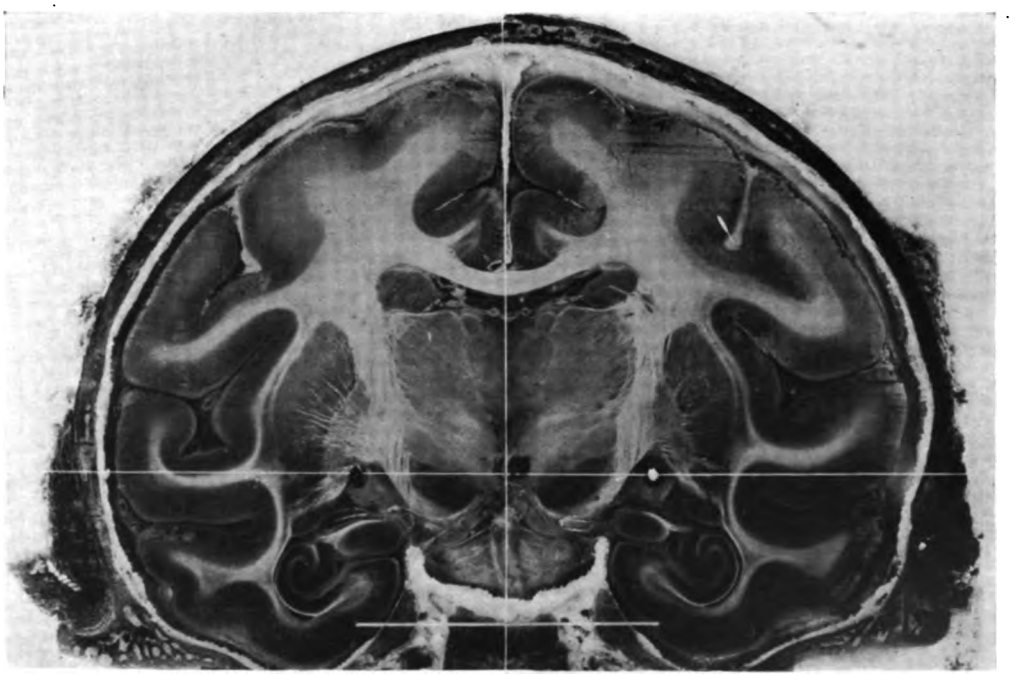

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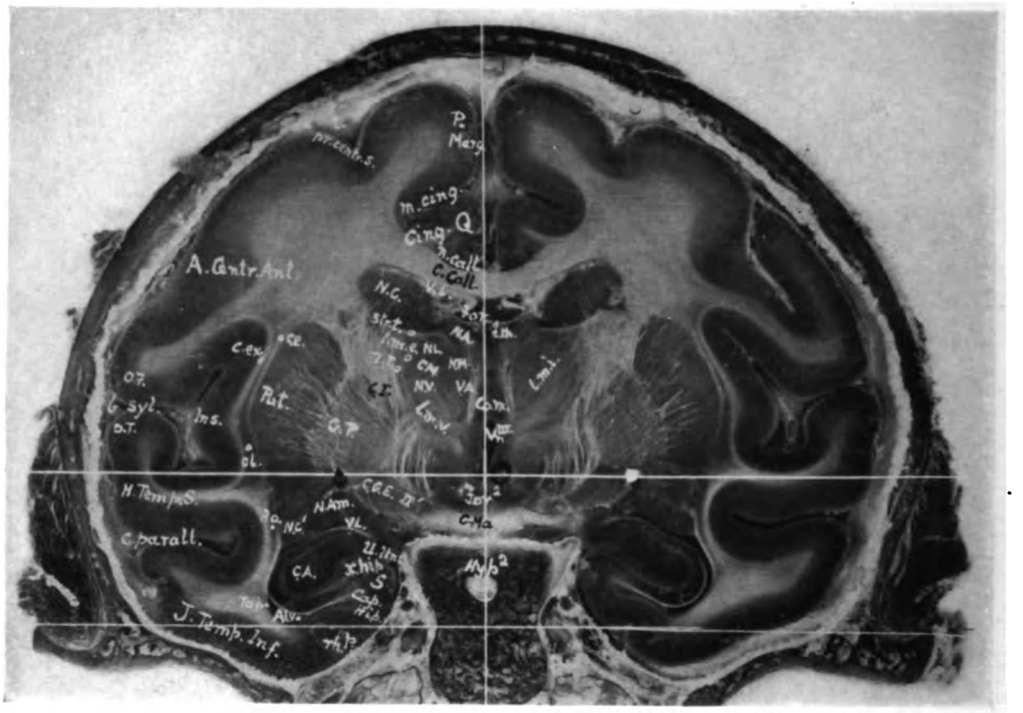

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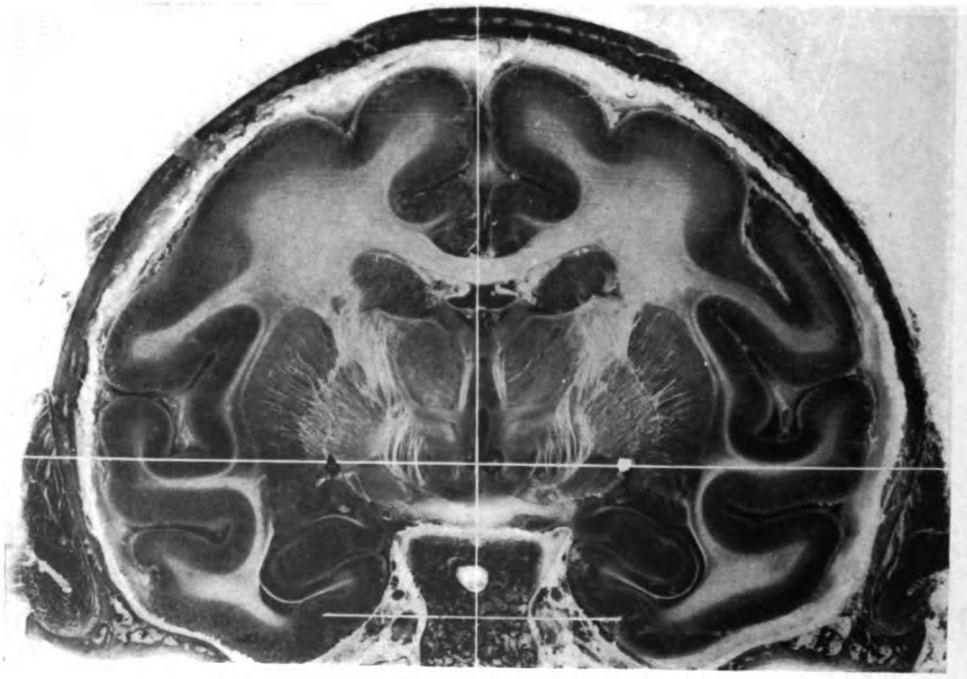

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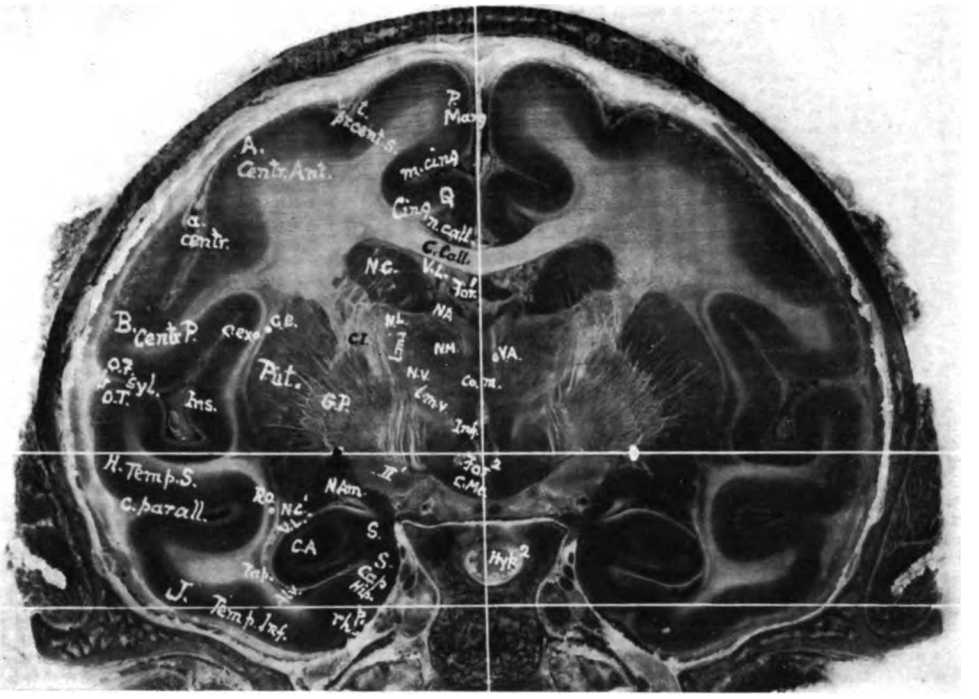

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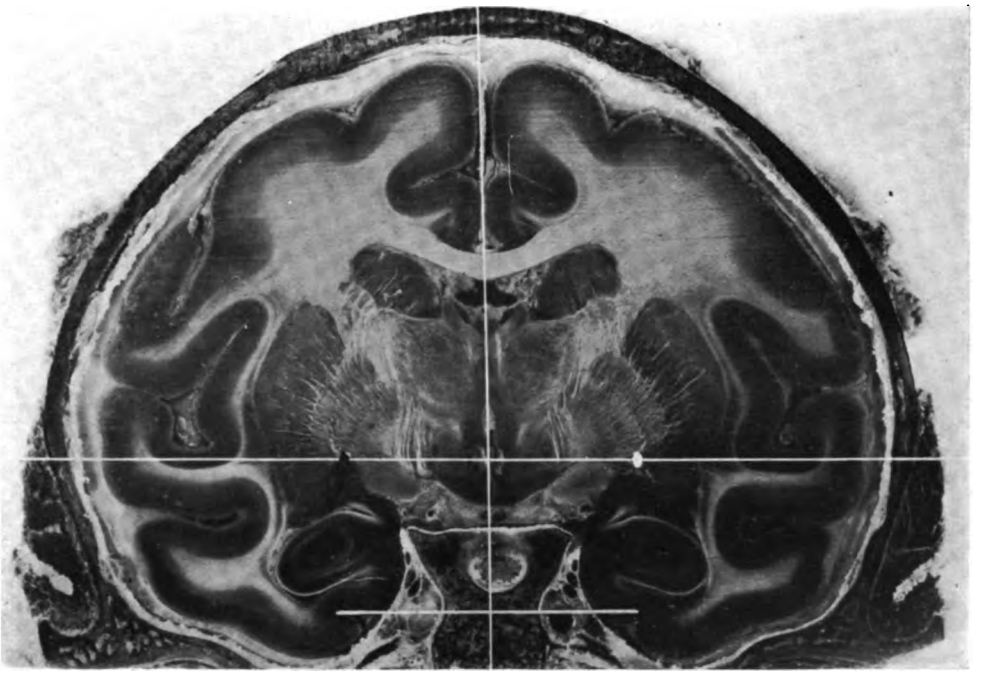

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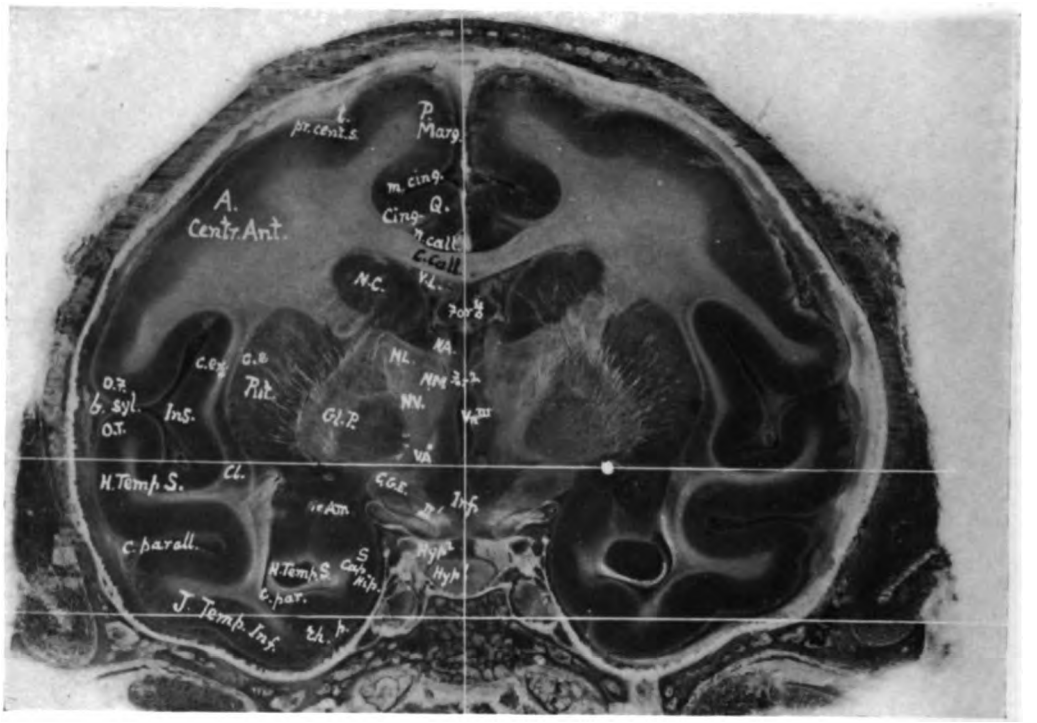

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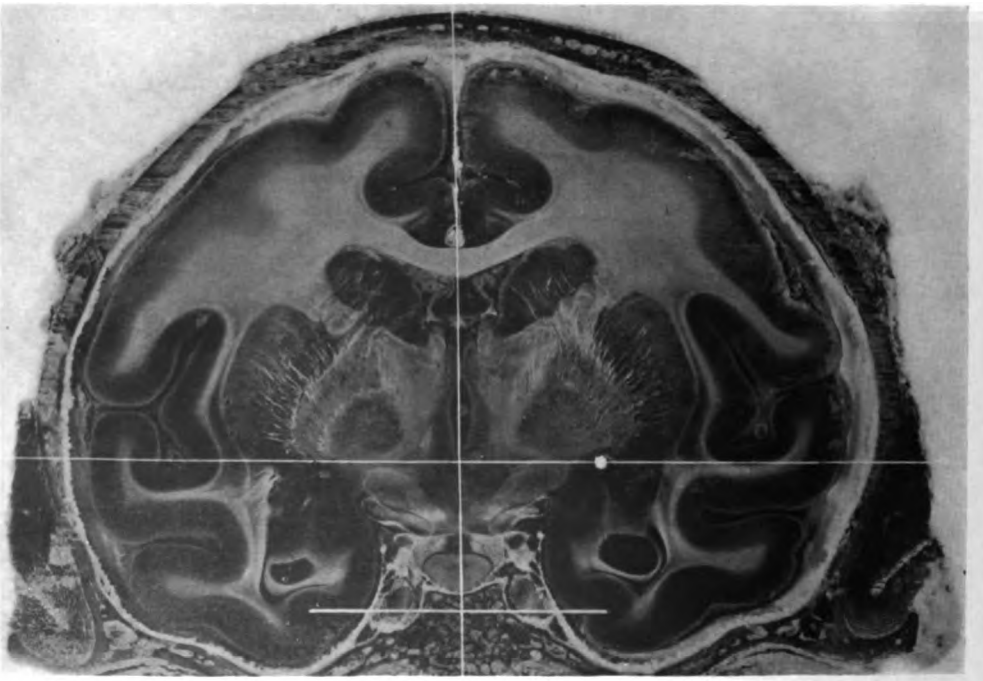

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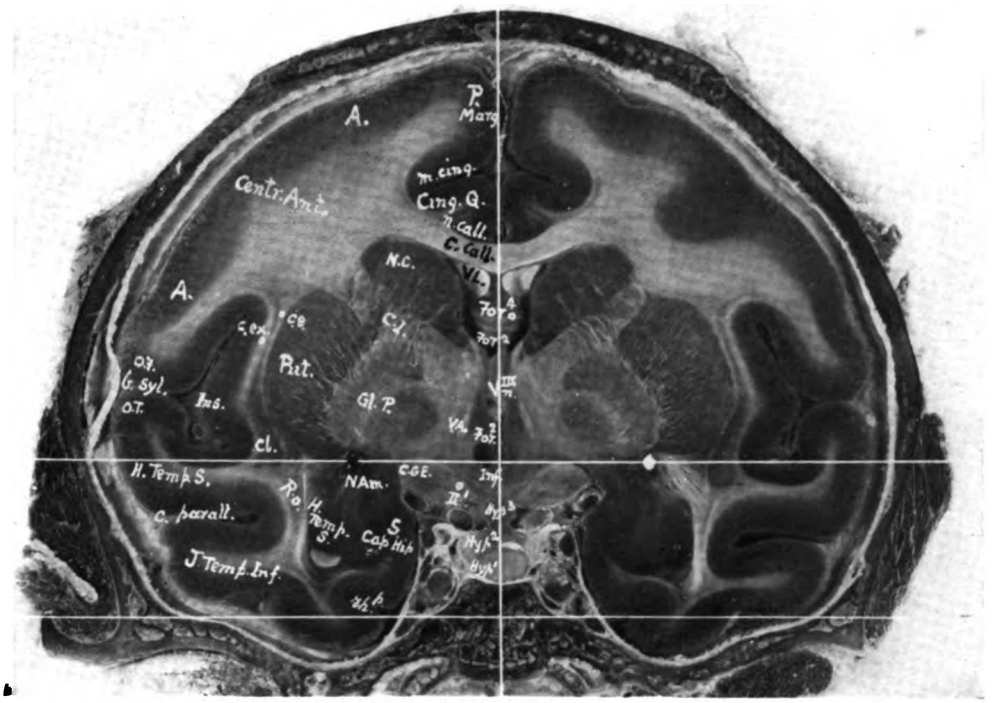

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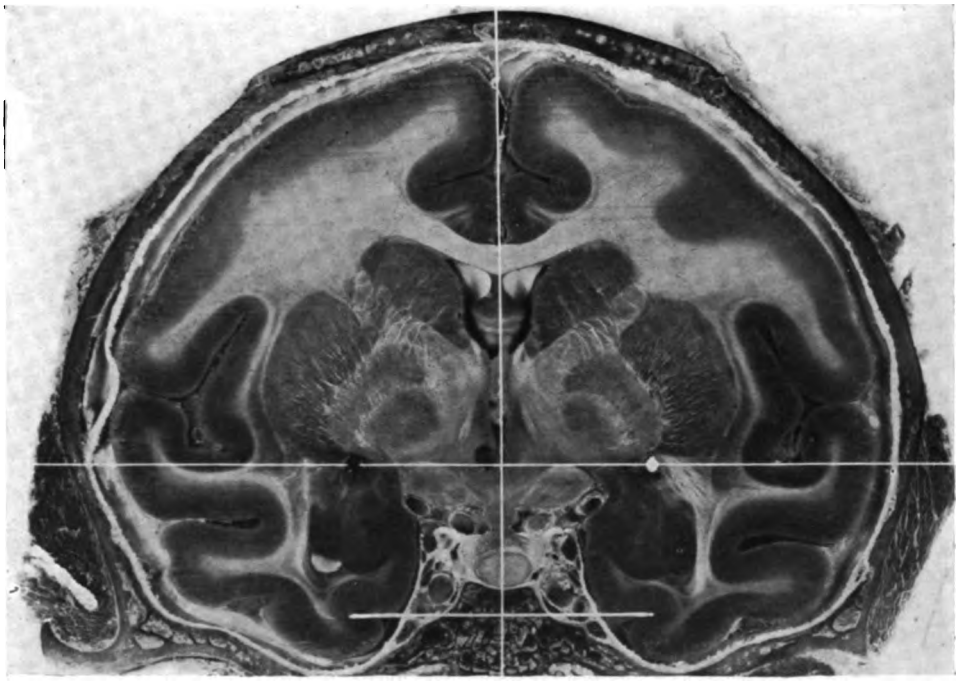

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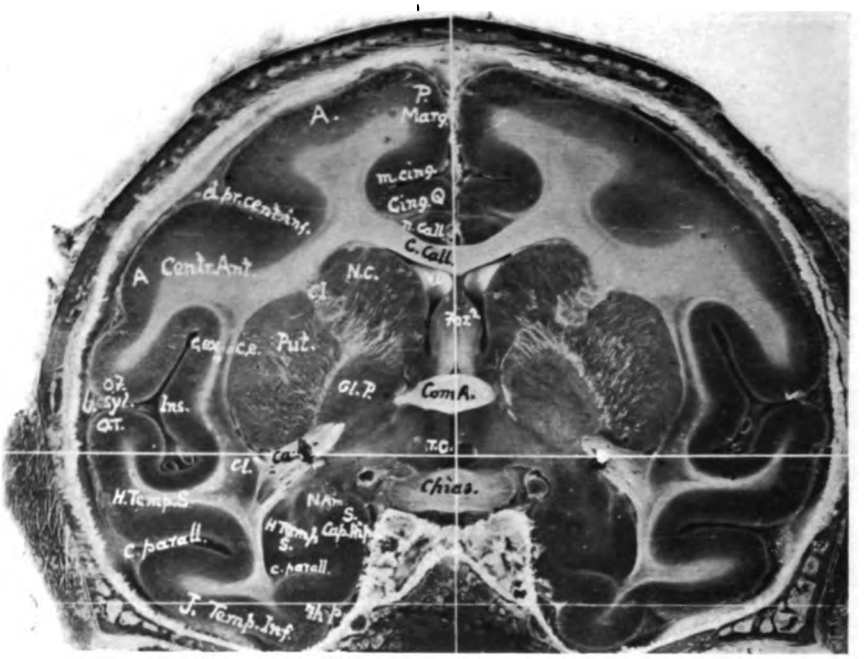

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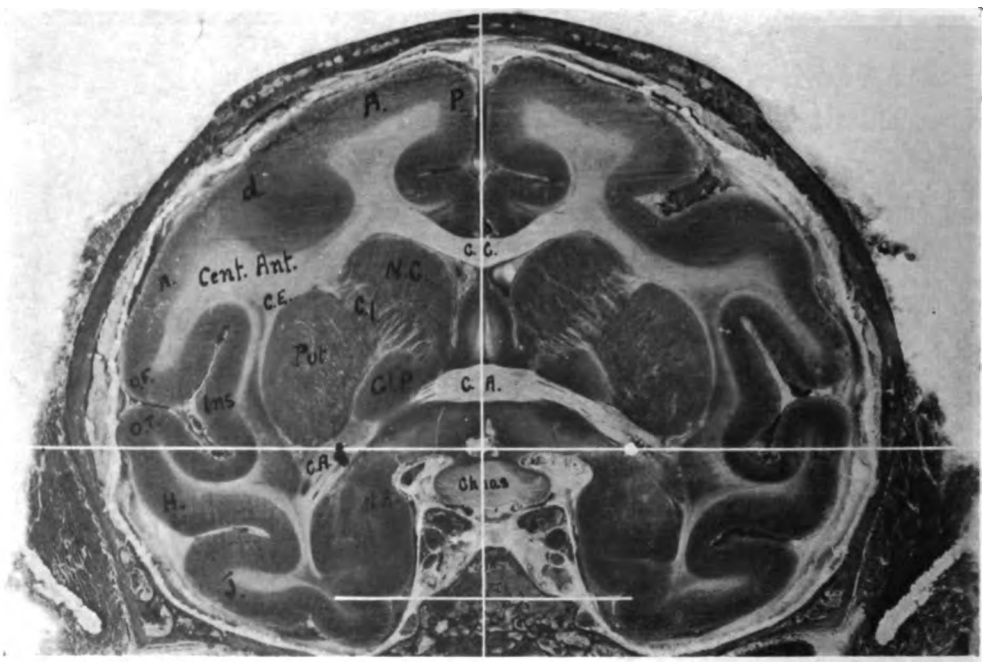

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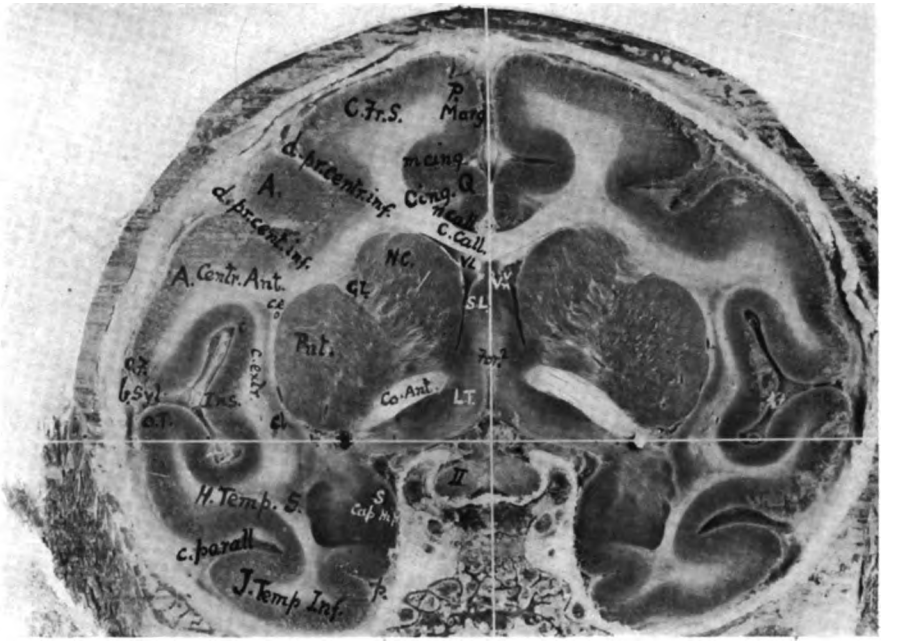

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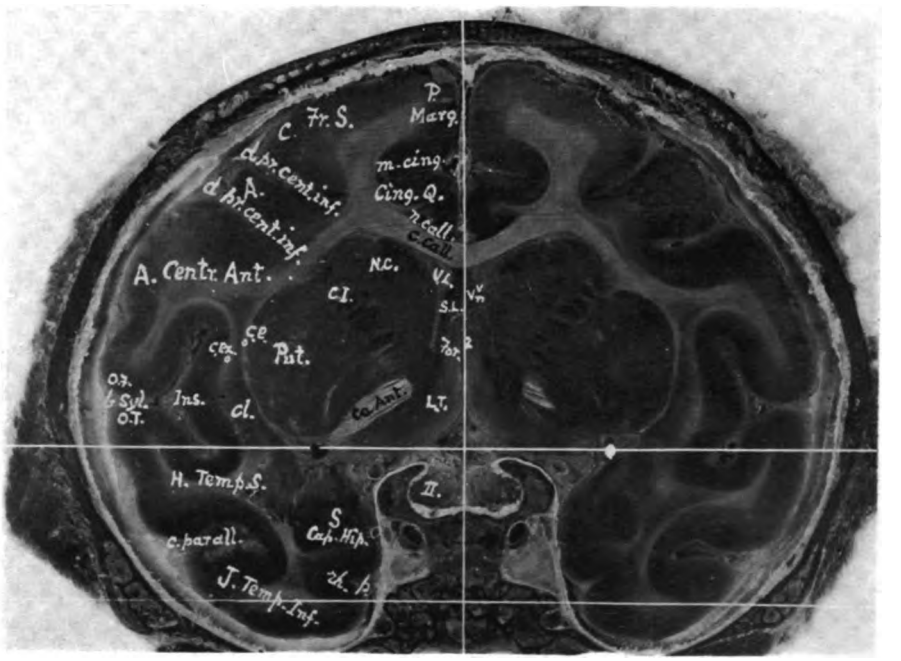

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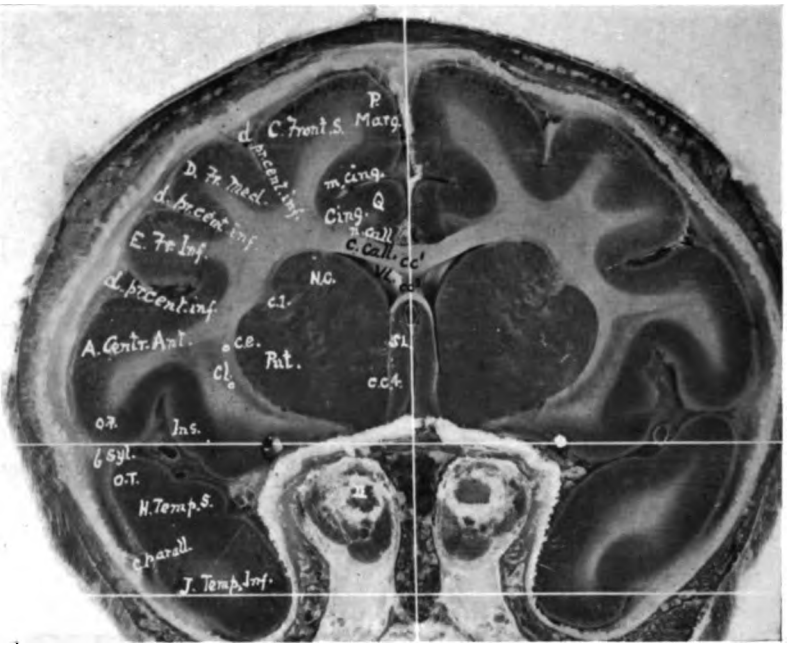

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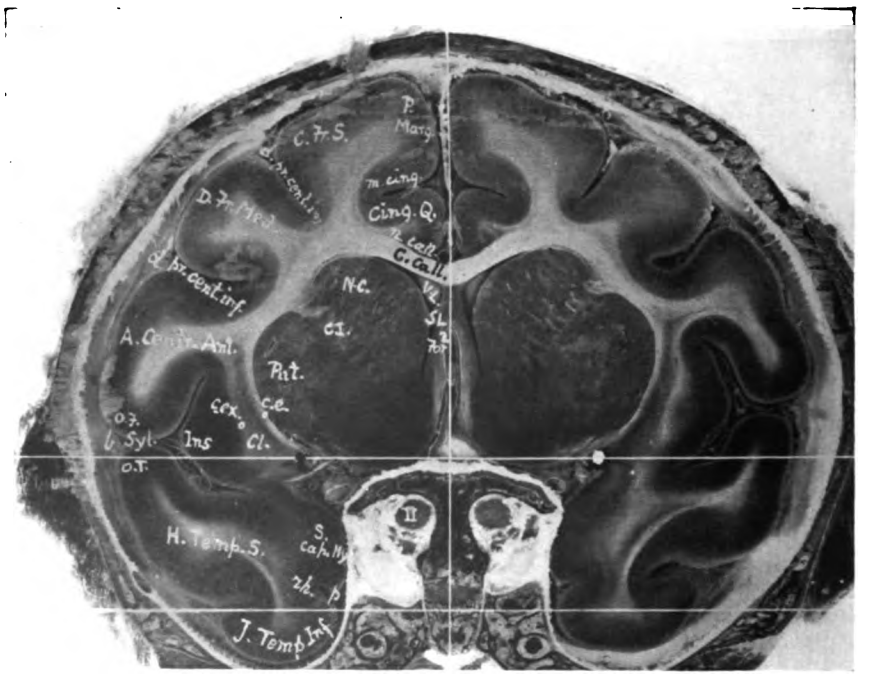

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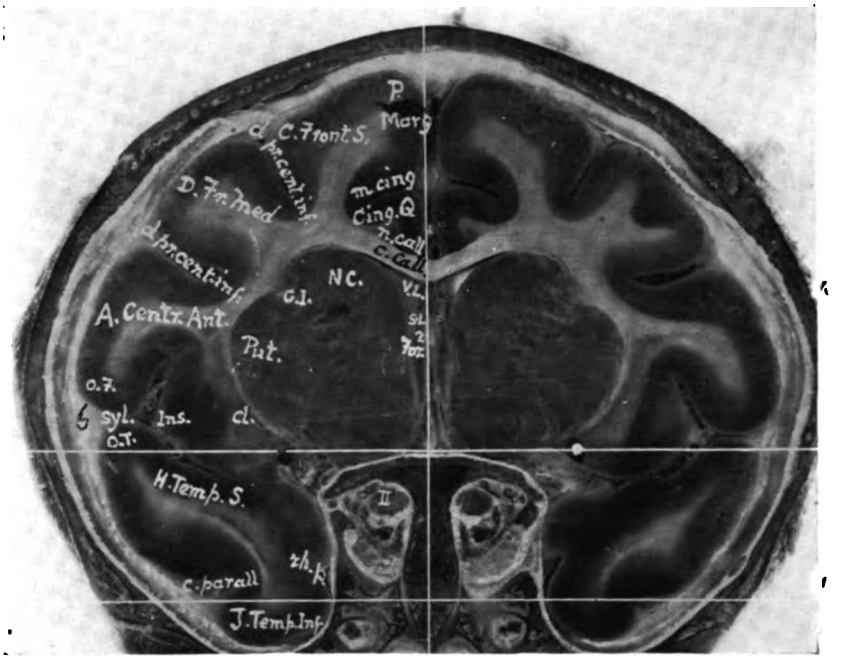

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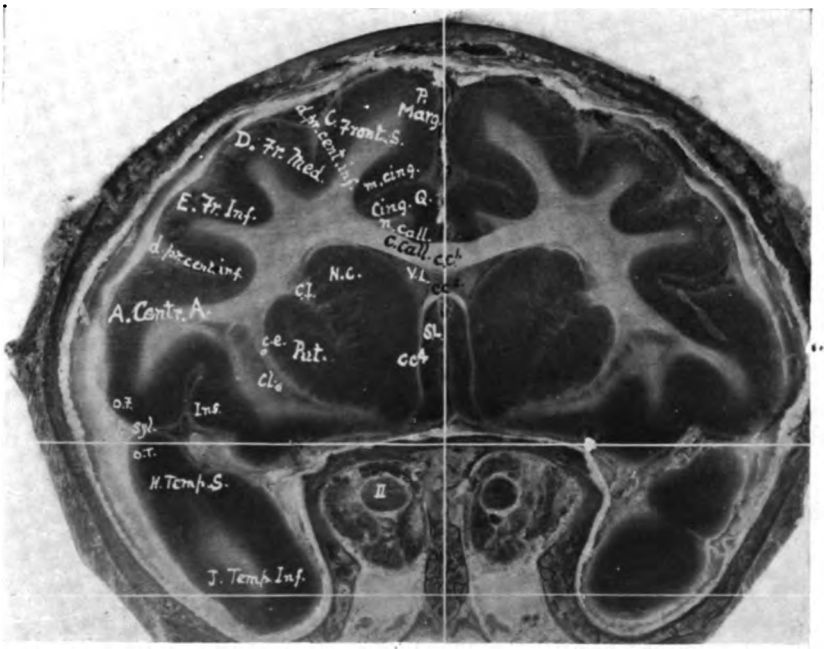

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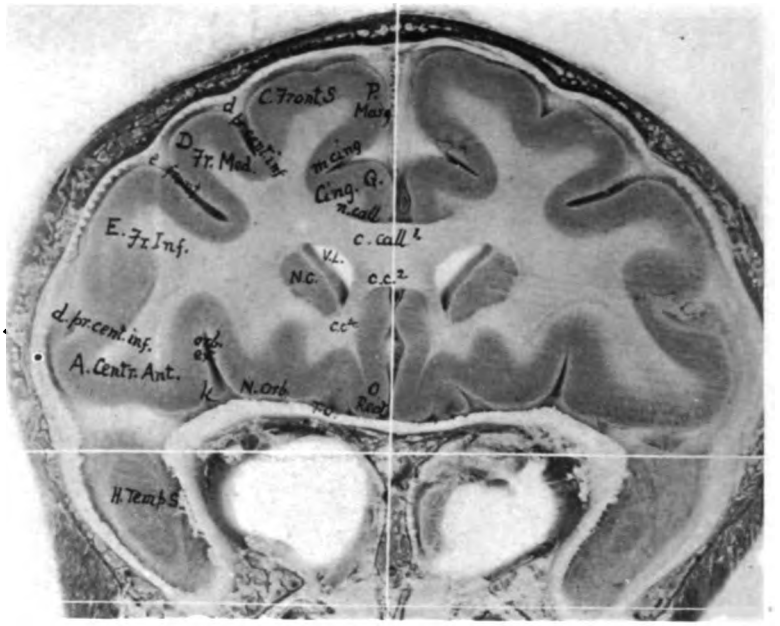

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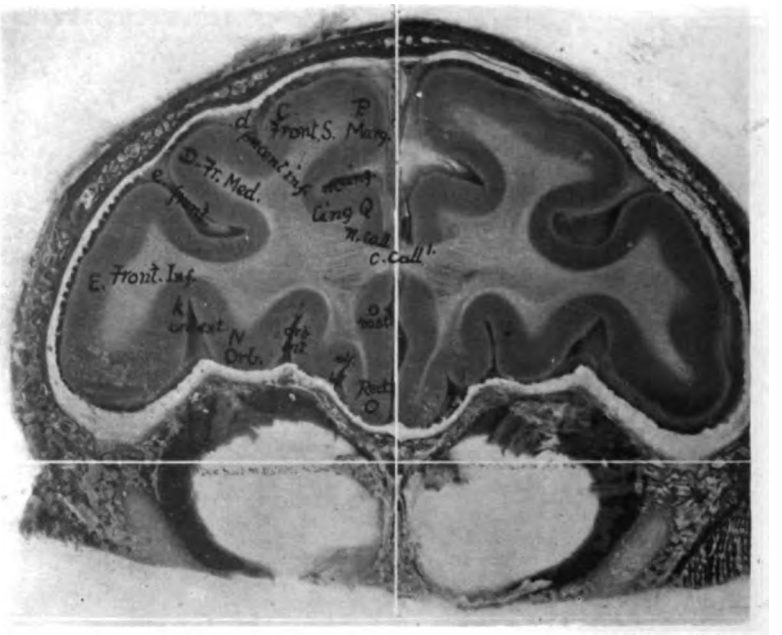

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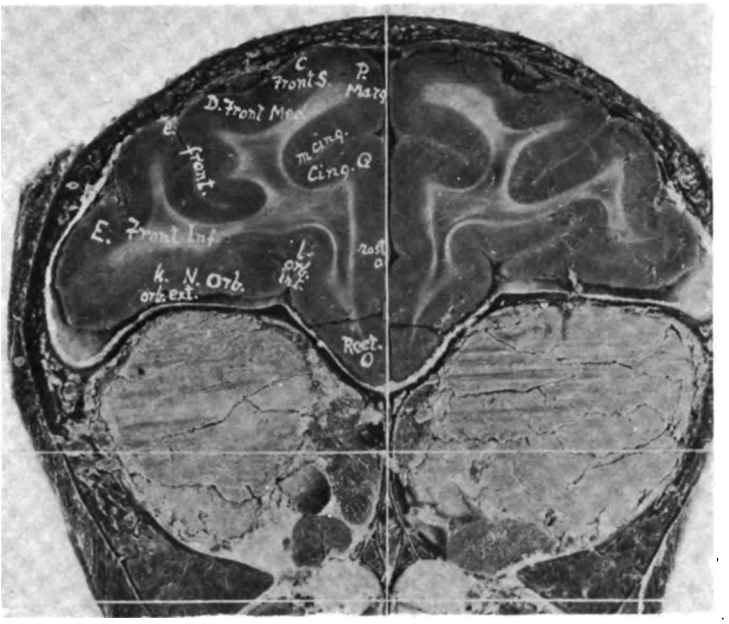

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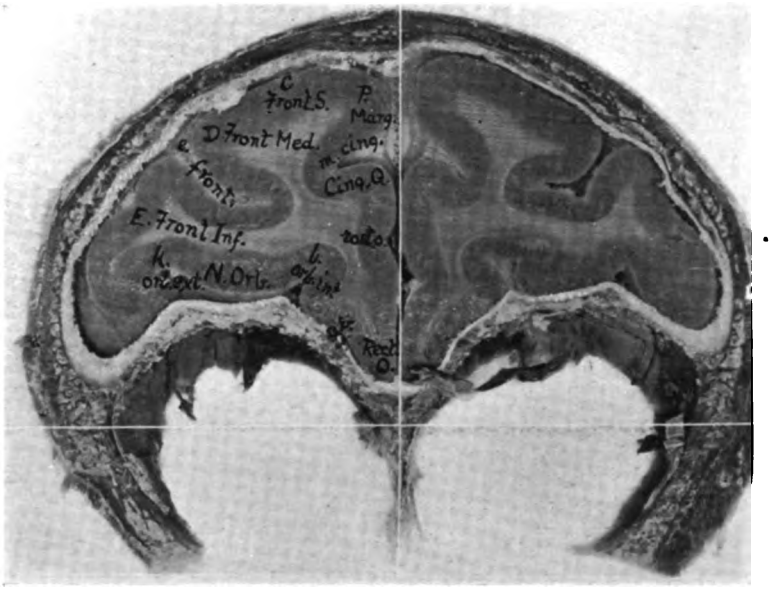

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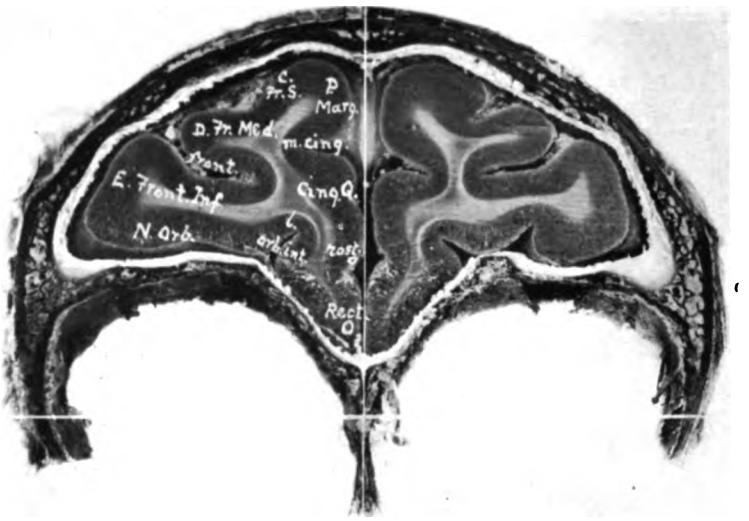

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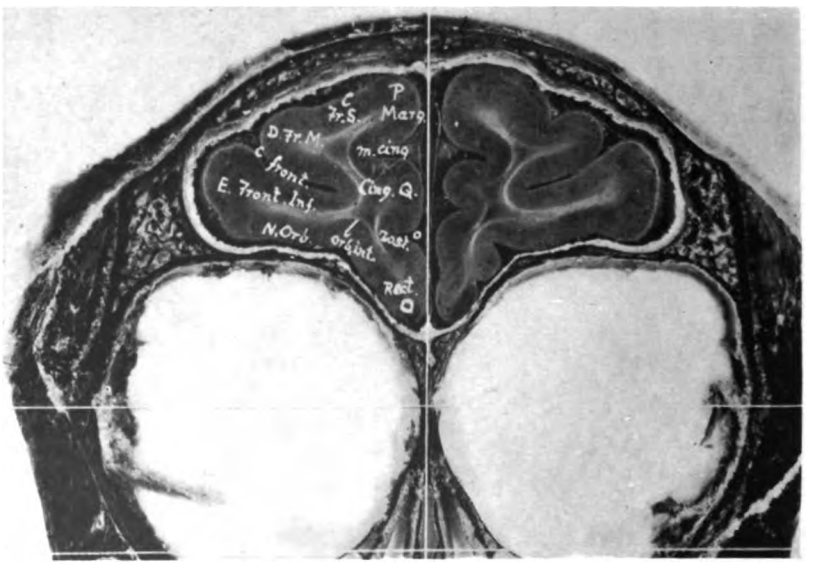

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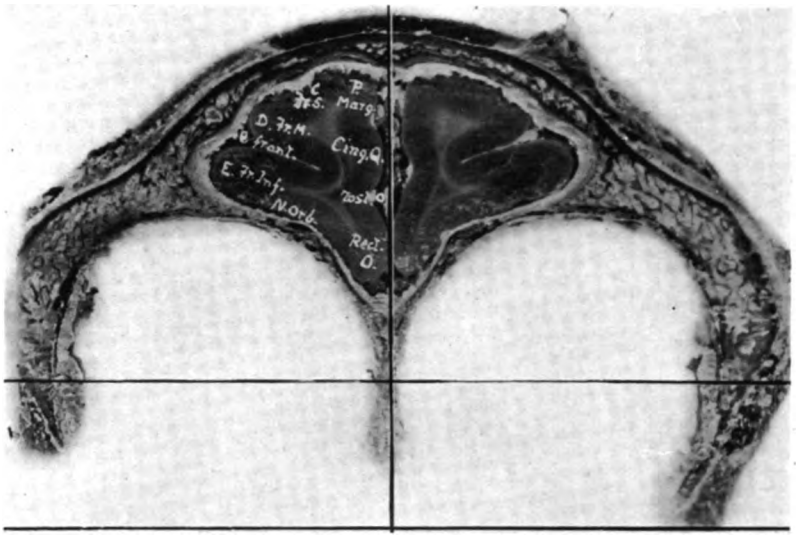

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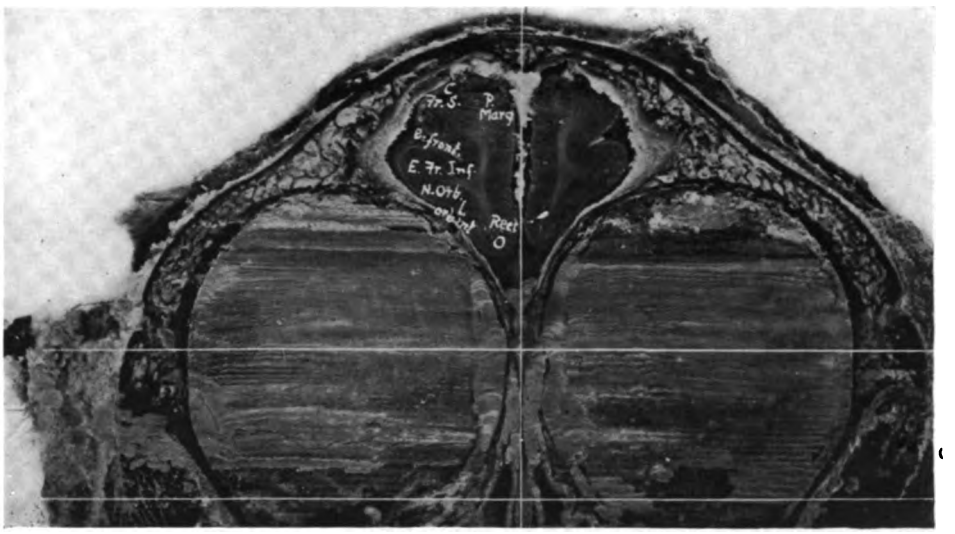

ANTERIOR FRONTAL LAMELLA. XL.

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Numerals)

is.
nterior.
osterior.

ssus lateralis.

dalis.
alis.
is.
s internus.
s externus.

is.

numerals)
rvi trigemini.
nervi acustici.
ryngeus.

nervi vagi.
nervi vagi.
s.
is.
nervi hypoglossi.

INITIALS and ABBREVIATIONS

Com. Cb.	Commissura cerebelli.
C. P.	Cornu posterius.
C. R.	Corpus restiforme.
Dec. L.	Decussatio lemniscorum.
F. B. / F. Cu.	Funiculus cuneatus.
F. G.	Funiculus gracilis.
Fl.	Fasciculus spino-cerebellaris posterior (Flechsig).
F. lat.	Funiculus lateralis.
F. l. d.	Fasciculus longitudinalis medialis.
F. l. i.	Fasciculus longitudinalis inferior.
F. p.	Funiculus posterior.
F. p. d.	Fasciculus predorsalis.
Go.	Fasciculus antero-lateralis superficialis (Gowers).
N. C. R.	Nucleus corporis restiformis.
N. Cu.	Nucleus funiculi cuneati.
P. c. s.	Brachium conjunctivum cerebelli.
Py.[1]	Tractus pyramidalis.
Py.[1] X.	Decussatio pyramidum.
R. O.	Radiatio occipito-thalamica.
R. sp.	Tractus rubro-spinalis.
S. G.	Substantia gelatinosa.
S. R.	Substantia Rolandi.
Tap.	Tapetum.
T. so.	Tractus solitarius.
V. L.	Ventriculus lateralis.
Vn. iv.	Ventriculus quartus.

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ABBREVIATIONS

C. A.	Cornu ammonis.
C. Call^{s}.	Corpus callosum (splenium).
C. Q. A.	Colliculus superior.
C. Q. P.	Colliculus inferior.
Ep.	Epiphysis.
E. T.	Eminentia medialis (teres).
Fl.	Fasciculus spino-cerebellaris posterior (Flechsig).
F. l. d.	Fasciculus longitudinalis medialis.
F l. i.	Fasciculus longitudinalis inferior.
F. p. d.	Fasciculus predorsalis.
Go.	Fasciculus antero-lateralis superficialis (Gowers).
L. c.	Locus ceruleus.
L. M.	Lemniscus medialis.
N. B.	Nucleus Becterew.
N. C.^{1}	Nucleus caudatus (cauda).
N. D.	Nucleus Deiters.
O. i.	Oliva inferior.
P. c. i.	Corpus restiforme.
P. c. m.	Brachium pontis.
P. c. s.	Brachium conjunctivum cerebelli.
Py^{1}.	Tractus pyramidalis.
R. O.	Radiatio occipito-thalamica.
R. sp.	Tractus rubro-spinalis.
S. g.	Substantia gelatinosa.
T. Ac.	Tuberculum acusticum.
Tap.	Tapetum.
T. sp.	Tractus tecto-spinalis.
V. L.	Ventriculus lateralis.
Vn. iv.	Ventriculus quartus.

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Go.	Fasciculus antero-lateralis superficialis (Gowers).
Gr. C.	Grisea centralis.
Hab.	Habenula.
Lin. inter.	Linea interauralis.
L. C.	Locus ceruleus.
L. L.	Lemniscus lateralis.
L. L. n. d.	Lemniscus lateralis, nucleus dorsalis.
L. L. n. m.	Lemniscus lateralis, nucleus medialis.
L. L. n. v.	Lemniscus lateralis, nucleus ventralis.
L. M.	Lemniscus medialis.
N. B.	Nucleus Becterew.
N. C.	Nucleus caudatus, caput.
N. C^{a}.	Nucleus caudatus, cauda.
N. D.	Nucleus Deiters.
N. D. T.	Nucleus dorsalis tegmenti.
N. V. gr.	Nucleus ventralis griseæ centralis.
N. V. T.	Nucleus ventralis tegmenti.
O. acc.	Oliva accesoria.
Oi.	Oliva inferior.
P. c. i.	Corpus restiforme.
P. c. m.	Brachium pontis.
P. c. s.	Brachium conjunctivum cerebelli.
Pulv.	Pulvinar.
Pul. l.	Pulvinar lateralis.
Pul. m.	Pulvinar medialis.
R. O.	Radiatio occipito-thalamica.
R. sp.	Tractus rubro-spinalis.
Str. t.	Stria terminalis.
Str. z.	Stratum zonale.
Sub.	Subiculum.
Tap.	Tapetum.
V. L.	Ventriculus lateralis.

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E. IV—VI

Gr. C.	Grisea centralis.
Hab.	Habenula.
L. L.	Lemniscus lateralis.
L. L. n. d.	Lemniscus lateralis, nucleus dorsalis.
L. L. n. m.	Lemniscus lateralis, nucleus medius.
L. L. n. v.	Lemniscus lateralis, nucleus ventralis.
L. M.	Lemniscus medialis.
L. m. e.	Lamina medullaris externa.
N. C.	Nucleus caudatus (caput).
N. C.[1]	Nucleus caudatus (cauda).
N. L.	Nucleus lateralis thalami.
N. M.	Nucleus medialis thalami.
N. D. T.	Nucleus dorsalis tegmenti.
N. V.	Nucleus ventralis thalami.
N. V. T.	Nucleus ventralis tegmenti.
O. I.	Oliva inferior.
P. c. m.	Brachium pontis.
P. c. s.	Brachium conjunctivum cerebelli.
Pl. ch.	Plexus choroideus.
Pul.	Pulvinar.
Py.[1]	Tractus pyramidalis.
R. O.	Radiatio occipito-thalamica.
Str. t.	Stria terminalis.
Str. z.	Stratum zonale thalami.
Sub.	Subiculum.
Tap.	Tapetum.
Tr. Cent. Teg.	Tractus centralis tegmenti.
V. L.	Ventriculus lateralis.
Vn.III	Ventriculus tertius.
Z. r.	Zona recticularis.

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ÆE. XVII—XL

BREVIATIONS

us callosum.
us callosum, genu.
us callosum, splenium.
us callosum, rostrum.
us callosum, columnæ.
ula externa.
sma.
ula interna.
strum.
missura anterior.
ix, columnæ anteriores.
us pallidus.
la.
ina terminalis.
eus amygdalæ.
eus caudatus (caput).
culum frontale.
culum temporale.
men.
um pellucidum.
r cinereum.
onum olfactorium.
riculus lateralis
riculus quintus

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	N. Am.	Nucleus amygdalæ.
	N. C.	Nucleus caudatus (caput).
	N. C. l.	Nucleus caudatus (cauda).
	N. f. l. d.	Nucleus fasciculi longitudinalis medialis.
n.	N. I.	Nucleus interpeduncularis.
l.	N. L.	Nucleus lateralis thalami.
	N. M.	Nucleus medialis thalami.
	N. Pf.	Nucleus parafascicularis thalami.
	N. Po.	Nuclei pontis.
	N. R.	Nucleus ruber.
	N. Sl.	Nucleus semilunaris thalami.
	N. Sm.	Nucleus submedianus thalami.
	N. V.	Nucleus ventralis thalami.
rior.	O. F.	Operculum frontale.
ert).	O. T.	Operculum temporale.
	P. c.	Pedunculus cerebri.
	P. c. m.	Brachium pontis.
	Pons.	Pons Varolii.
	P. P. C.	Pes pedunculi cerebri.
	Pulv.	Pulvinar thalami.
	Put.	Putamen.
	R. O.	Radiatio occipito-thalamica.
	Srt.	Substantia reticularis.
	Str. t.	Stria terminalis.
	Sub.	Subiculum.
	Tap.	Tapetum.
	T. th.	Taenia thalami.
	V. A.	Fasciculus thalamo-mammillaris (Vicq d'Azyr).
	V. L.	Ventriculus lateralis.
	Vn. III.	Ventriculus tertius.
	Vn. V.	Ventriculus quintus.
	Z. i.	Zona incerta.
	Z. r.	Zona reticularis.

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CEREBRUM

	GYRI. (Capital letters)	ABBREVIATIONS
A.	Gyrus centralis anterior.	Cent. A.
B.	Gyrus centralis posterior.	Cent. P.
C.	Gyrus frontalis superior.	Front. S.
D.	Gyrus frontalis medius.	Front. M.
E.	Gyrus frontalis inferior.	Front. I.
F.	Gyrus angularis.	Ang.
G.	Gyrus postparietalis.	Po. par.
H.	Gyrus temporalis superior.	Temp. S.
J.	Gyrus temporalis inferior.	Temp. I.
K.	Gyrus occipito-temporalis.	Occ. T.
L.	Gyrus occipitalis superior.	Occ. S.
M.	Gyrus occipitalis inferior.	Occ. I.
N.	Gyrus orbitalis.	Orb.
O.	Gyrus rectus.	Rect.
P.	Gyrus marginalis.	Marg.
Q.	Gyrus callosus.	Call.
R.	Gyrus hippocampi.	Hip.
S.	Gyrus hippocampi (caput).	Cap. Hip.
T.	Gyrus lingualis.	Ling.
U.	Gyrus uncinaus.	Un.
V.	Gyrus cuneatus.	Cun.
W.	Gyrus precuneatus.	Pr. C.

	SULCI. (Small letters)	ABBREVIATIONS
a.	Sulcus centralis.	Cent.
b.	Sulcus sylvianus.	Syl.
c.	Sulcus parallel.	Parall.
d.	Sulcus precentralis inferior.	Pr. inf.
e.	Sulcus frontalis.	Fr.
f.	Sulcus intraparietalis.	Intr. p.
g.	Sulcus parieto-occipitalis externus.	P. occ. ex.
h.	Sulcus occipito-temporalis.	Occ. t.
i.	Sulcus occipitalis lateralis.	Occ. lat.
j.	Sulcus occipitalis inferior.	Occ. inf.
k.	Sulcus orbitalis externus.	Or. ex.
l.	Sulcus orbitalis internus.	Or. int.

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m.	Sulcus cinguli.	Cing.
n.	Sulcus callosus.	Call.
o.	Sulcus rostralis.	Ros.
p.	Sulcus rhinalis.	Rh.
q.	Sulcus calcarinus.	Calc.
r.	Sulcus parieto-occipitalis internus.	P. occ. int.
s.	Sulcus collateralis.	Coll.
t.	Sulcus precentralis superior.	Pr. c. s.
u.	Sulcus postcentralis.	Po. c.
v.	Sulcus subparietalis.	Sub. par.
w.	Sulcus olfactorius.	Olf.
x.	Fissura hippocampi.	Hip.

LOBULI. (Numerals)	ABBREVIATIONS
1. Lingula.	Ling.
2. Lobulus centralis.	Cent.
3. Lobulus culminis.	Cul.
4. Lobulus clivi.	Cliv.
5. Folium vermis.	Fol.
6. Tuber vermis.	Tub.
7. Pyramis.	Py.
8. Uvula.	Uv.
9. Nodulus.	Nod.
10. Lobulus paramesialis.	Par. mes.
11. Lobulus pennatus anterior.	Pen. A.
12. Lobulus pennatus posterior.	Pen. P.
13. Paraflocculus.	Pfl.
13^1. Paraflocculus, processus lateralis (petrosal lobule).	Pfl. p. l.
14. Flocculus.	Fl.

SULCI	ABBREVIATIONS
16. Sulcus precentralis.	Pr. c.
17. Sulcus postcentralis.	Po. c.
18. Sulcus preclivalis (fissura prima).	Pr. cl.
19. Sulcus postclivalis (rachis pennæ).	Po. cl.
20. Sulcus horizontalis.	Hor.
21. Sulcus postpyramidalis.	Po. py.
22. Sulcus prepyramidalis.	Pr. py.
23. Sulcus post nodularis.	Po. nod.
24. Sulcus paraflocculi superior.	Pfl. s.
25. Sulcus paraflocculi inferior.	Pfl. i.
27. Sulcus paramesialis internus.	Pm. i.
28. Sulcus paramesialis externus.	Pm. e.

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CRANIAL NERVES. (Roman numerals)

I. Nervus olfactorius.
I¹. Tractus nervi olfactorii.
II. Nervus opticus.
II¹. Tractus nervi optici.
II². Chiasma nervorum opticorum.
III. Nervus oculomotor.
III¹. Nucleus nervi oculomotoris.
IV. Nervus trochlearis.
IV¹. Nucleus nervi trochlearis.
IV². Decussatio nervorum trochlearium.
V. Nervus trigeminus.
V¹. Radix mesencephalicus nervi trigemini.
V². Radix spinalis nervi trigemini.
V³. Nucleus mesencephalicus nervi trigemini.
V⁴. Nucleus motor minor nervi trigemini.
V⁵. Nucleus motor major nervi trigemini.
V⁶. Nucleus sensilis nervi trigemini.
VI. Nervus abducens.
VI¹. Nucleus nervi abducentis.
VII. Nervus facialis.
VII¹. Radix nervi facialis.
VII². Genu nervi facialis.
VII³. Nucleus nervi facialis.
VIII. Nervus acusticus.
VIII¹. Nucleus dorsalis nervi acustici.
VIII². (N. D.) Nucleus Deiters.
VIII³. (N. B.) Nucleus Bechterew.
VIII⁴. Tuberculum acusticum (Tub. Ac.).
IX. Nervus glossopharyngeus.
IX¹. Nucleus nervi glossopharyngei.
X. Nervus vagus.
X¹. Nucleus dorsalis nervi vagi.
X². Tractus solitarius nervi vagi.
X³. Nucleus ambiguus nervi vagi.
XI. Nervus accessorius.
XI¹. Nucleus nervi accessorii.
XII. Nervus hypoglossus.
XII¹. Nucleus nervi hypoglossi.

ABBREVIATIONS

Al. Alveus.
Aq. Aqueductus cerebri.
Br. A. Brachium anticum.
Br. P. Brachium posticum.
C. A. Cornu ammonis.

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C. Call.	Corpus callosum.
C. Call^{1}.	Corpus callosum, genu.
C. Call^{2}.	Corpus callosum, splenium.
C. Call^{3}.	Corpus callosum, rostrum.
C. Call^{4}.	Corpus callosum, columnæ.
C. e.	Capsula externa.
C. ex.	Capsula extrema.
C. G. E.	Corpus geniculatum externum.
C. G. I.	Corpus geniculatum internum.
Chias.	Chiasma.
Cl.	Claustrum.
C. M.	Centre médian (Luys').
C. Mam.	Corpus mammillare.
Com. A.	Commissura anterior.
Com. Cb.	Commissura cerebelli.
Co. m. M.	Massa intermedia.
Co. Po.	Commissura posterior.
Co. CQP.	Commissura colliculi inferioris.
C. P.	Cornu posterius.
C. Q. A.	Colliculus superior.
C. Q. P.	Colliculus inferior.
C. R.	Corpus restiforme.
C. Sth.	Corpus subthalamicum.
Dec. Br.	Decussatio brachiorum conjunctivorum.
Dec. L.	Decussatio lemniscorum.
Ep.	Epiphysis.
E. T.	Eminentia medialis (teres).
F. B. F. Cu.	Fasciculus cuneatus.
F. G.	Fasciculus gracilis.
Fl.	Fasciculus spino-cerebellaris posterior (Flechsig).
F. lat.	Funiculus lateralis.
F. l. d.	Fasciculus longitudinalis medialis.
F. l. i.	Fasciculus longitudinalis inferior.
Flo.	Flocculus.
F. M.	Fasciculus retroflexus (Meynert).
For.	Fornix.
For^{1}.	Fornix, columnæ horizontales.
For^{2}.	Fornix, columnæ anteriores.
For^{3}.	Fornix, fimbria.
For^{4}.	Fornix, nucleus proprius.
For^{5}.	Fornix, columnæ posteriores.
F. p.	Funiculus posterior.
F. p. d.	Fasciculus predorsalis.
G. D.	Gyrus dentatus.

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G. Hab.	Ganglion habenulæ.
G. P. / Gl. P.	Globus pallidus.
G. Pi.	Glandula pinealis.
Go.	Fasciculus anterolateralis superficialis (Gowers).
Gr. C.	Grisea centralis.
Hab.	Habenula.
Hyp^1.	Hypophysis pars anterior.
Hyp^2.	Hypophysis pars posterior.
Hyp^3.	Hypophysis pars medialis.
Inf.	Infundibulum.
Ins.	Insula.
L. C.	Locus ceruleus.
L. L.	Lemniscus lateralis.
L. L. n. d.	Lemniscus lateralis, nucleus dorsalis.
L. L. n. m.	Lemniscus lateralis, nucleus medius.
L. L. n. v.	Lemniscus lateralis, nucleus ventralis.
L. M.	Lemniscus medialis.
L. m. e.	Lamina medullaris externa.
L. m. i.	Lamina medullaris interna.
L. m. v.	Lamina medullaris ventralis.
L. N.	Locus niger.
L. T.	Lamina terminalis.
Mass. Int.	Massa intermedia.
N. A.	Nucleus anterior thalami.
N. Am.	Nucleus amygdalæ.
N. Amb.	Nucleus ambiguus.
N. B.	Nucleus Bechterew.
N. C.	Nucleus caudatus (caput).
$N. C^1$.	Nucleus caudatus (cauda).
N. C. R.	Nucleus corporis restiformis.
N. Cu.	Nucleus cuneatus.
N. Gr.	Nucleus gracilis.
N. D.	Nucleus Deiters.
N. D. T.	Nucleus dorsalis tegmenti.
N. f. l. d.	Nucleus fasciculi longitudinalis medialis.
N. L.	Nucleus lateralis thalami.
N. M.	Nucleus medialis thalami.
N. Pf.	Nucleus parafascicularis thalami.
N. R.	Nucleus ruber.
N. Sl.	Nucleus semilunaris thalami.
N. Sm.	Nucleus submedialis thalami.
N. V.	Nucleus ventralis thalami.
N. V. gr.	Nucleus ventralis griseæ centralis.
N. V. T.	Nucleus ventralis tegmenti.

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O. acc.	Oliva accessoria.
O. F.	Operculum frontale.
Oi.	Oliva inferior.
O. T.	Operculum temporale.
P. C.	Pedunculus cerebri.
Pc. i.	Corpus restiforme.
P. c. m.	Brachium pontis.
P. c. s.	Brachium conjunctivum cerebelli.
Pl. ch.	Plexus choroideus.
Pons.	Pons Varolii.
P. P. C.	Pes pedunculi cerebri.
Pulv.	Pulvinar thalami.
Pul. l.	Pulvinar lateralis thalami.
Pul. m.	Pulvinar medialis thalami.
Put.	Putamen.
Py^1.	Tractus pyramidalis.
Py^1X.	Decussatio pyramidum.
R. O.	Radiatio occipito-thalamica.
R. sp.	Tractus rubro-spinalis.
S. g.	Substantia gelatinosa.
S. L.	Septum pellucidum.
S. R.	Substantia Rolandi.
S. rt.	Substantia reticularis.
Str. t.	Stria terminalis.
Str. z.	Stratum zonale.
Sub.	Subiculum.
T. Ac.	Tuberculum acusticum.
Tap.	Tapetum.
T. C.	Tuber cinereum.
T. O.	Trigonum olfactorium.
Tr. cent. teg.	Tractus centralis tegmenti.
T. So.	Tractus solitarius.
T. sp.	Tractus tecto-spinalis.
t. th.	Tænia thalami.
V. A.	Fasciculus thalamo-mamillaris (Vicq. d'Azyr).
V. L.	Ventriculus lateralis.
Vn. III.	Ventriculus tertius.
Vn. IV.	Ventriculus quartus.
Vn. V.	Ventriculus quintus.
Z. i.	Zona incerta.
Z. r.	Zona reticularis.

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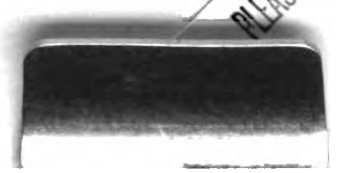

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